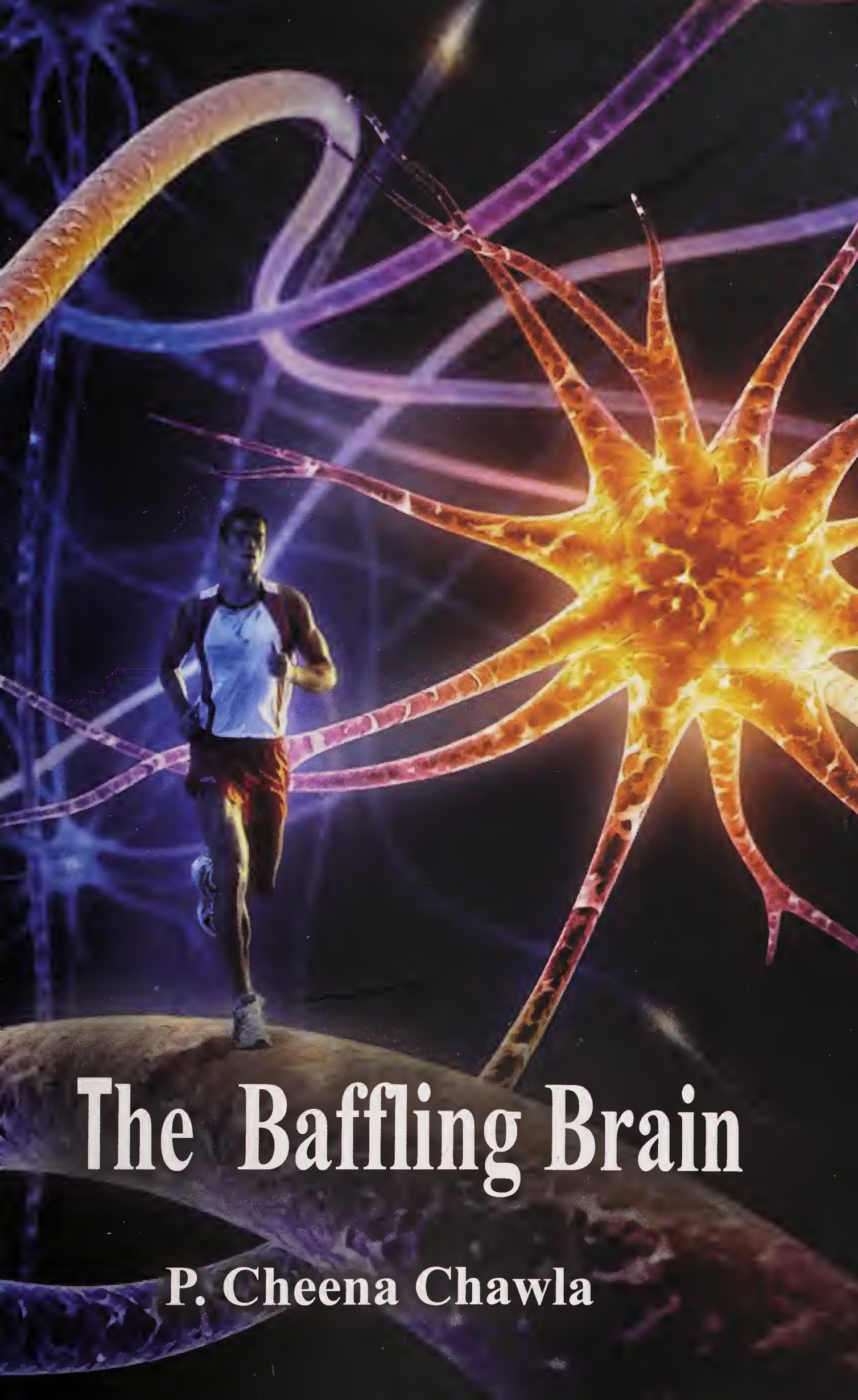

The Baffling Brain

P. Cheena Chawla

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Cheena Chawla

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Preface

The purpose of writing this book is to bring to light the present breathtaking knowledge on the functional intricacies of the human brain. This includes the basic information about the brain parts and their individual well defined functions, the importance of neural connections for the transmission of a nerve impulse and how the release of neurotransmitters at the junctions between two neurons in a normal brain differ from those affected by some disorder. To further enrich readers' knowledge, some amazing facts about the human brain have been unfolded like the size of brain does not reflect one's intelligence, playing computer games does improve one's multi-tasking abilities, children who learn to play a musical instrument have better spatial reasoning skills etc.

The evolution of the human brain, and the definite roles of the right and left hemispheres is indeed quite interesting. How the brain circuitry develops in primordial brain cells in a fetus to form a complete human brain has been discussed, along with the dual effect of one's genetic material and the role of early environment crucial in infant brain development. The neurological milestones in a baby that define the brain activities, at different stages, of a developing brain are, therefore, important. Various childhood afflictions of the human brain like autism, cerebral palsy and dyslexia are known but not clearly understood by many, especially with regard to the parental influence in the management of such brain anomalies that show the socio-cultural importance of managing these neuronal diseases in the young. Similarly, how the key brain circuits in children do not develop properly resulting in Attention Deficit Hyperactivity Disorder (ADHD) finds a place in this book. Preschool education is thus important in brain development of a child.

The breakdown of the neuronal machinery in psychiatric and psychosomatic disorders namely, schizophrenia, bipolar affective disorder, manic depression, obsessive compulsive disorder and even drug addiction is explained for the benefit of readers. Similarly, the functional errors in neural networks occurring in other disorders like Alzheimer's disease, Parkinson's disease, Huntington's chorea, epilepsy and multiple sclerosis have been explained. With the deciphering of the human genome, many genes responsible for the occurrence of brain disorders have come to light. Information on such defective genes responsible for a particular brain disorder is provided to enrich readers' knowledge. Since there is no definite cure for many anomalies of the human brain, the role of parents, spouse and other family members in patient care has been highlighted, for it assumes importance in the effective management of these disorders. Information about various brain scanning/ medical imaging techniques like EEG, PET scan, CAT scan and MRI that play an important role in the diagnosis of brain disorders has been given.

Though modern day stressful life could be the root cause of anomalies in the human brain, sometimes quite early in life, yet a good night sleep can do wonders in bringing back the alertness of mind and rejuvenating the brain. Similarly, the role of other stress busters like various yogic and meditative exercises, and mind-relaxation techniques in improving blood circulation in the human brain have been mentioned. These natural techniques can miraculously play a key role in reversing many disorders of the brain for which ironically, the neuroscientists are still struggling to find a cure. In this context, what is normal sleep pattern and why dreams occur has been explained, in contrast with sleep disorders and occurrence of insomnia.

Readers' views are welcome.

Acknowledgements

Playing with words to make any seemingly difficult subject 'easy-to-understand' is the hallmark of creative writing, and indulging in this art is indeed pleasurable for it satiates my inner urge to communicate S&T information among masses in a language they understand. Of course, the ability to write in a simple language, minus most of the technical jargon of that subject, becomes more and more easy as the subject in all its details is first understood and secondly, as the target reader is constantly kept in mind for whom this exercise is initiated.

The challenge of writing a popular science book invariably becomes an enjoyable experience for me as while penning down the script I become one with the consciousness of my prospective readers. As this happens during all my creative writing work, I strangely experience an effortless flow of knowledge about the subject, from deep within, taking the shape of sentences and paragraphs, filling page after page, to form chapters that finally this gives birth to a manuscript! It happened yet again as I wrote this book.

For giving me this pleasure and privilege, I profusely thank the Director, Publications Division, Ministry of Information & Broadcasting, Government of India, New Delhi. I whole-heartedly acknowledge the sincere efforts of the Editor, Mrs. S. Manjula and her team for editing the script and coordinating all production work. Although the script went through a long incubation period before it finally got ready for printing, I extend my appreciation and gratitude to all whose efforts have gone into publishing this book.

My sincere thanks are due to my daughter Ms. Gunnika Chawla, a student of class 8th of Genesis Global School, Noida for making the beautiful illustrations for this book that enrich the

contents and make understanding for this otherwise difficult subject simpler. I salute the young artist in her for making many concepts 'alive' in this book that would not have been so exciting to read otherwise.

My husband, Dr. Anil Kumar Chawla deserves special thanks for supporting me all through and standing by me as I took upon me the task of writing this book. I acknowledge, with pleasant memories, the support of my son, Aman and daughter Gunnika, for without their understanding and faith in me this book could not have been written.

- Dr. Cheena Chawla

Dedicated to all scientists, surgeons, doctors and professionals, intellectually inclined to explore the depths of the organ that has made us superior to all life forms, and yet remains least understood—the Human Brain

Contents

1

A Bundle of Grey Matter

The vast repertoire of life forms existing on our planet, including us, are all unique components of nature that are held together through a common thread called 'Life'. But every life form, be it a single-celled bacterium or a complex living system of a multi-cellular organism, is bestowed with unique identifying features that make it stand out from the rest.

As human beings, we are greatly blessed for we singularly possess a highly complex 1.5 kg organ that sits comfortably inside our skull and fills the space between our ears. Thanks to this amazingly wonderful organ, we could understand the myriad mysteries of galaxies and unravel the structure of atoms, and have unfolded the secrets of the genetic code, each a daunting challenge on its own. This seat of intellect called 'brain' has bestowed us with an unparalleled ability to think rationally, a quality that no other life form, however big and mighty on this planet can boast of.

The unique position of human beings in the entire living world owes greatly to this highly sophisticated organ which is the key to human thinking, learning and all higher mental functions besides being involved in several mundane tasks such as sensing the environment, regulating body temperature and controlling body movements among others. The puzzle of how the human brain allows us to perceive, behave, think, feel, and control our environment poses a daunting challenge that has baffled scientists over the years.

The important aspects of this puzzle are to firstly understand how over millions of years the primitive nervous system of our

early ancestors evolved into an organ that has made us today the most adaptable and intelligent organism on the planet. Secondly, the challenge before us is to unravel the mystery of how a single fertilized egg cell develops the intricate structure of the brain during the course of embryonic development in the womb. Unfolding how the mature human brain continues to modify itself at cellular and molecular levels to acquire new skills and information in an ever-changing world is yet another intriguing challenge that we face today.

The Evolution of Brain

To understand how the human brain differs from the brain of other animals, let us take a look at how this organ evolved over the years in different animals including us. Each and every being inhabiting our planet today has had a history of millions of years of evolution during which that species was subjected to survival battles with its competitors. In fact, the exposure to many hostile environments allowed the more fit species to survive while the unfit beings that were unable to cope up with the adversities were simply wiped out. Basically, there occur genetic alterations called 'mutations' to give rise to new adaptations in a life form to suit a given environment. In this way, life forms that emerge victorious in adapting themselves to their environment are more likely to survive and pass on their genes to the next generation.

As different organisms climbed the evolutionary ladder over millions of years, their brains also got evolved. Although the basic building blocks of this organ — the brain cells — are almost identical in all animals, the evolution of brains of insects, fish, reptiles, birds and mammals has been dependent on particular tasks controlled by specific regions of the brain that were crucial to the survival of that species. For example, the nervous system of a jellyfish is very simple as it comprises an undifferentiated network of nerve cells or neurons that primarily serve to coordinate the animal's swimming motions. Worms have a simple nervous system, which includes a distinct brain that is connected to groups of neurons

organized as 'nerve cords' running along the length of their body. Interestingly, even with their brain removed, worms are able to perform many types of body functions that include locomotion, mating, burrowing, feeding, and even maze learning!

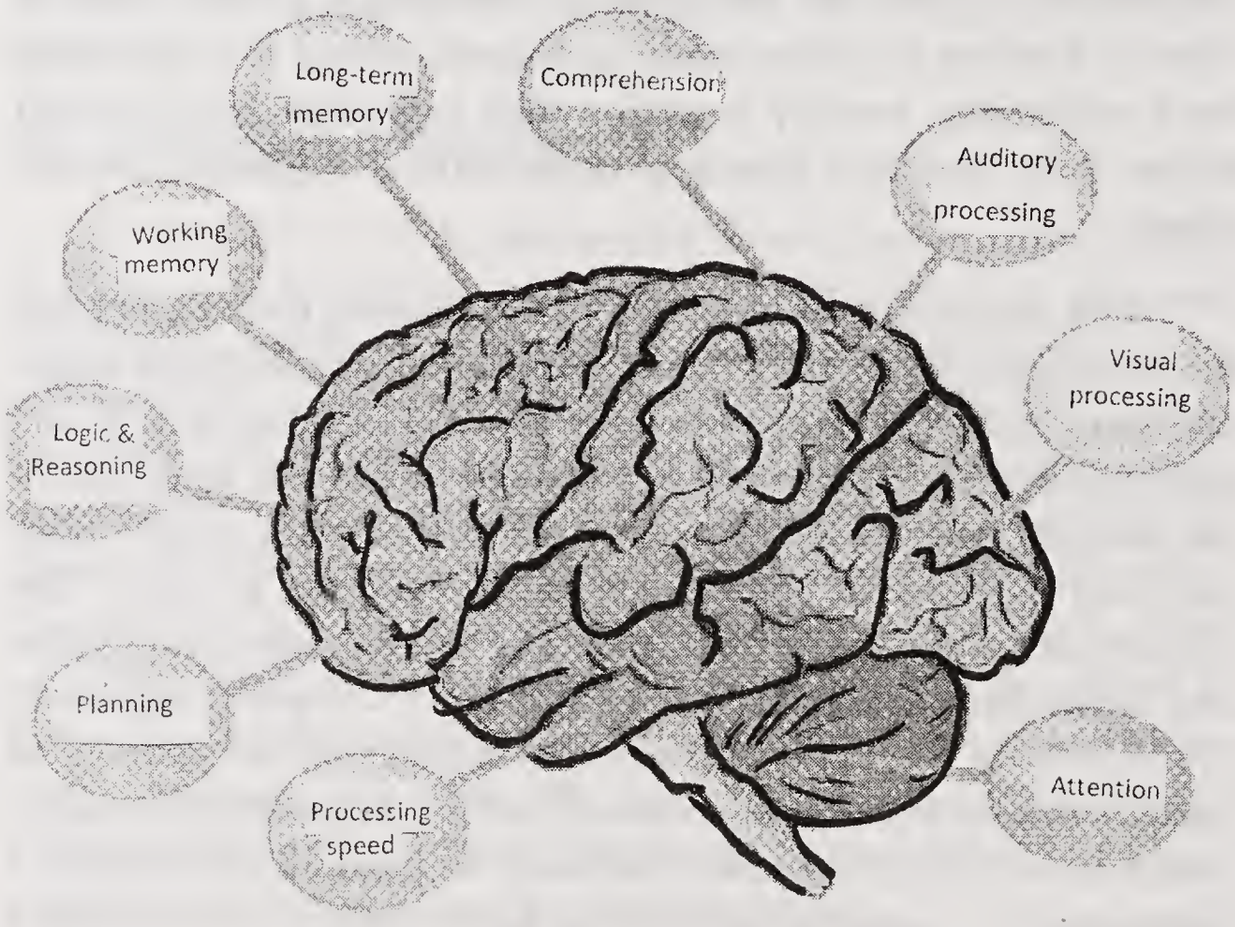
Brain complexity in insects is seen as a giant fiber system that allows rapid conduction of nerve impulses, connecting parts of the brain to specific muscles in legs or wings. Such neural connections permit, for example, the cockroach to dart away as soon as it senses any movements or objects around it. Insects thus have astounding sensory reception than any other life form that makes them the most abundant multi-cellular organisms on our planet.

The complexity of brain and its functioning increases as one moves up the evolutionary ladder. The brain becomes much larger and more complex as we move to vertebrates such as fish and amphibians. The spinal cord is protected within the vertebrae of the backbone where lies the nerve fibres that orchestrate a busy two-way highway of communication categorized as motor and sensory pathways. Move up further and see the brains of reptiles and birds, and they appear to be still more complex, especially those areas of the brain are more developed that are devoted to specific senses. For example, crocodiles have huge olfactory bulbs, which is the area of the brain that deals with smell. Then comes a wide variety of mammalian species, having varying brain shapes and sizes.

Superiority of the Human Brain

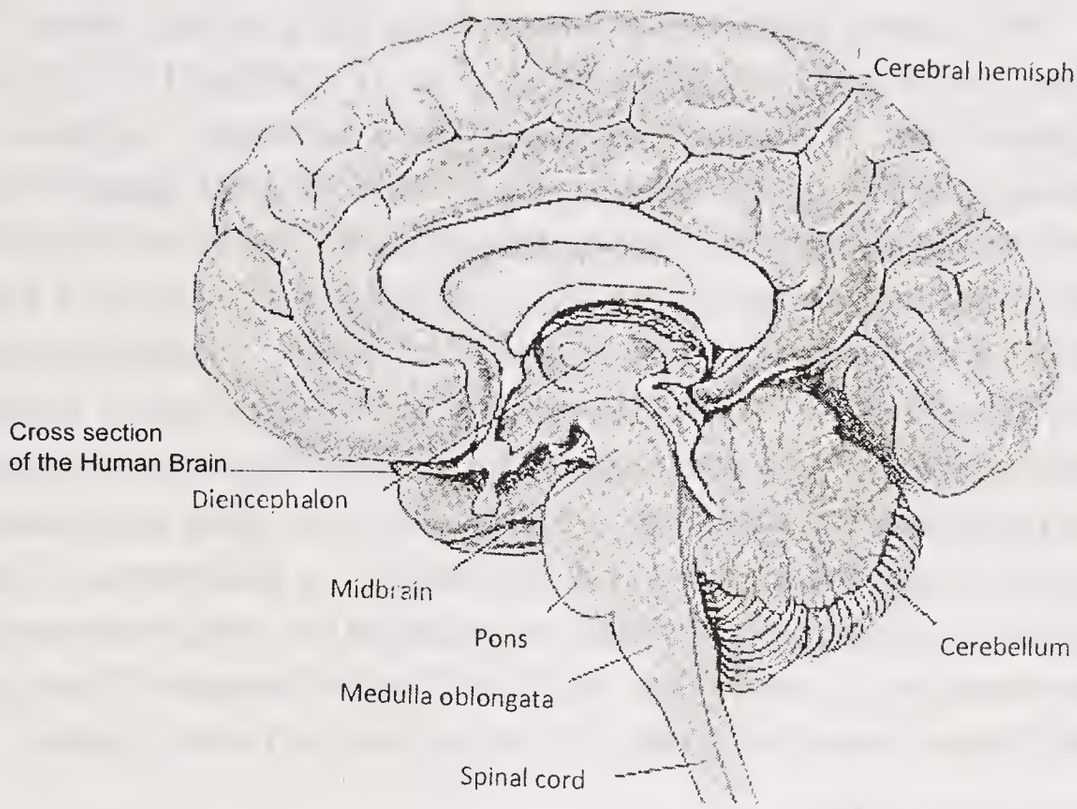
The brain in vertebrates basically comprises the three major parts: the hindbrain, midbrain, and forebrain. Cerebellum (Latin for little brain) is a region of the hind brain. Among mammals, the brain has two new structures: 'neocerebellum' that is added to the cerebellum and the 'neocortex' that grows out of the front of the forebrain, called the prefrontal and frontal lobes. Human beings are blessed with large convoluted mass of this grey neural matter comprising neocerebellar and neocortical tissue in the form of extensive

foldings, valleys and ridges, which increase the surface area of the cortex and allow a maximum amount of grey matter to be packed within the confines of the skull. This is the reason why human beings enjoy the largest ratio of brain weight to body weight as compared to that of any other life form. Other intelligent mammals like dolphins and chimpanzees also have convoluted brains as compared to the smooth brains of lesser intelligent animals.

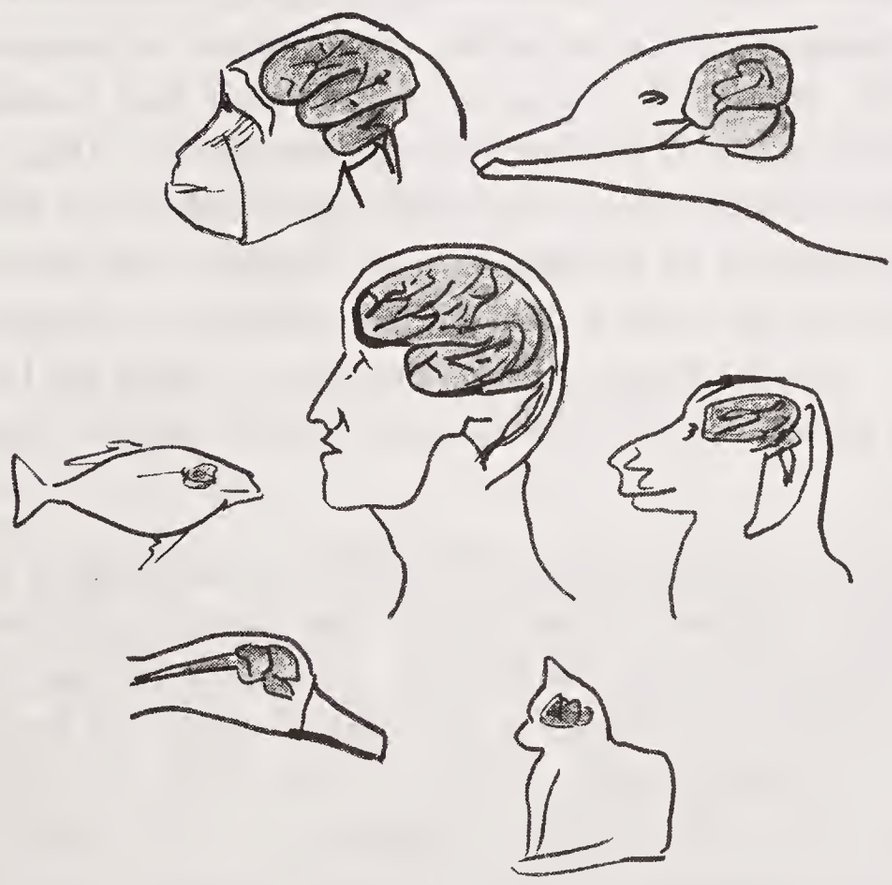


We are superior to other life forms, thanks to the unparalleled functions of the human brain.

The unique abilities of the human brain – the powers of speech and written language, the power of thinking, observing, planning, reasoning, imagining etc., reside in the cerebral cortex and this makes us what we are, different from other animals. Although, the size of the brain does define the intelligence of that being, it is actually the brain weight in relation to body weight that is a good indication of intelligence. It is for this reason again that the tiny hummingbird having a brain weighing less than a gram is remarkably equipped with a marvellous variety of behaviours!



Cross section of the human brain



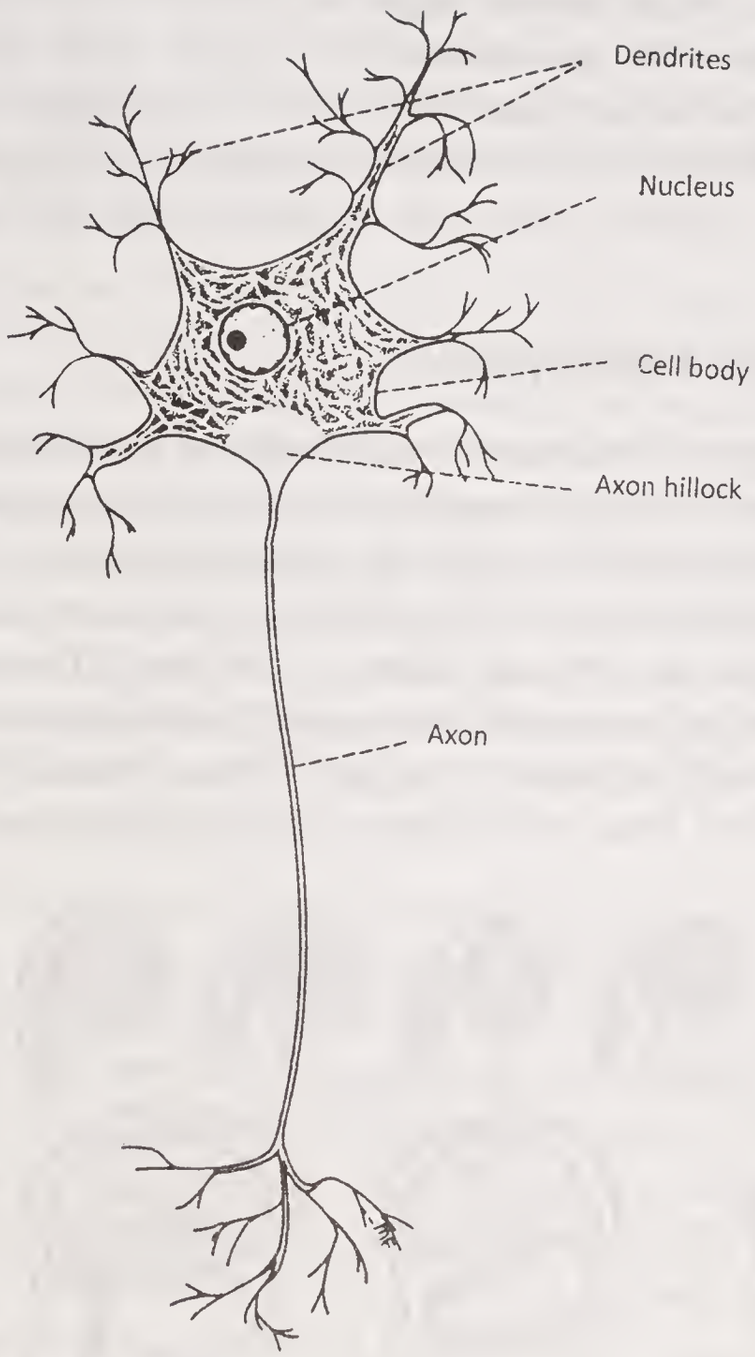
Brains of different animals evolved in support of survival of that species

The human brain has evolved from 400g organ, about 3-4 million years ago, to the present size of 1500g (1.5 kg) that comprises about 10 billion specialized neurons, capable of receiving, processing and relaying the electrochemical signals which control all our sensations, actions, thoughts and emotions. Scientists believe that human evolution has exceptionally involved a large number of mutations in a large number of genes, including several genes involved in brain development. Interestingly, human intelligence is not just attributed to the number of neurons that the brain possesses but more importantly, it is how these neurons are organized and interconnected that makes a difference. More connections mean more vibrant communication links between the interconnecting neurons that results in myriad complex functions of the human brain that make this organ unique to our species.

Brain's Building Blocks

Neurons are the building blocks of the brain. All neurons share common structural features. A neuron basically has a cell body or 'soma' that contains the nucleus which, in turn, houses the complete genetic blueprint of the organism. The nucleus is surrounded by cytoplasm, the chemical 'soup' of the cell that contains the organelles essential to the functioning of the neuron. Thus, neurons are similar to other body cells, except that unlike most other cells they rarely divide to reproduce new neurons. For carrying out specialized tasks, every neuron has complex communicative channels – the structures called 'dendrites'– which are like many tentacles of an antenna system that receive signals from other neurons.

As soon as a dendrite is stimulated on receiving a chemical signal from a neuron connected to it, this signal travels rapidly as an electrochemical impulse from the cell body moving along the neuron's single axon where it gets picked up by the dendrites of other neurons. Although the size of a neuron's body is usually small, the length of its axon could be considerable, which means that one neuron may influence the firing of another neuron connected to it but present far away.



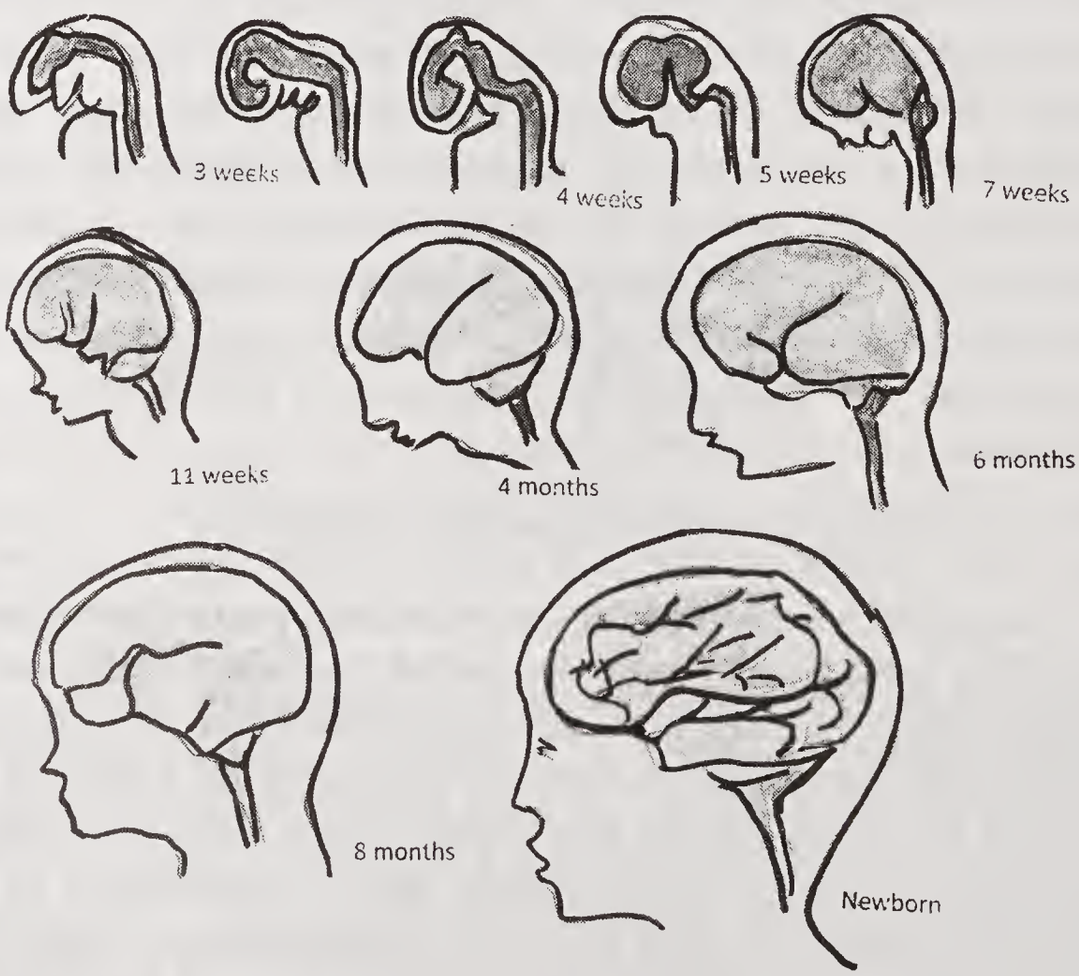
Structure of neuron—The building block of brain

The points where two interconnected neurons are joined with each other are special junctions called 'synapses'. Known as 'synaptic junctions', they normally connect the axon of one neuron with the dendrites of another. Unbelievably, a typical neuron in the cortex of the human brain has about 10,000 synapses, which constitutes a complex wiring system that is unparalleled to the complexity of even the most advanced supercomputers! Basically. this intricate wiring of neurons in the human brain bestows it the most amazing abilities this organ possesses.

The brain comprises not only the excitable cells called the neurons but also the non-excitable, support cells called the 'neuroglia' that in Latin means 'nerve glue' which largely comprise the glial cells. Besides neurons and glial cells, the brain has many blood vessels – arteries, veins and capillaries that also serve the brain tissue.

Human Brain Development

The pioneering work on brain development and function by Roger Sperry revealed that the connections of the nervous system are specified in the organism's genes, an important finding for which ne won the Nobel Prize in 1981. But how do countless neural connections form an intricate wiring in the brain? For example, how does a particular neuron know to which muscle fiber it must connect? The work of David Hubel and Torsten Wiesel, who both shared the Nobel Prize with Sperry, showed that neural axons



Human brain development: From embryo to adult brain

present in the visual cortex actually 'compete' for space in this region of the brain, which was dependent on the amount and type of sensory stimulation carried by these axons. It is now known that the fine-tuning of neural connections in a developing embryo begins to take place in the womb itself.

Nonetheless, the interactive postnatal experience of the external world is crucial for normal development of senses and nervous systems in mammals. For example, cats who have one eye sewn shut at birth lose all ability to see with this eye when it is opened several months later. The same applies to humans. Eye infections in newborn infants have been seen to result in cloudy lenses and corneas causing blindness, even though the retina and visual nervous system were normal at the time of birth. Thus, immature animals and children are unable to develop normal vision if they are not exposed to a sharply focused visual world during this period of brain development.

The normal development of the brain thus depends on a critical interaction between genetic inheritance/inborn tendencies and environmental/learning experiences. Although our genes specify the general structure of the central nervous system, the sensory stimulations based on environmental inputs help to fine-tune the neural connections. It was in 1906 when it was observed that in embryonic nerve tissue, some neurons appeared to be degenerating and dying. But how does the nervous system know which connections to retain and which to eliminate?

A child's brain is fundamentally different from an adult brain. During embryonic development itself, as the fertilized egg embarks upon its journey towards non-stop divisions to form a mass of cells that further begin to differentiate into specific tissues based on the plan written in the genetic blueprint, the first recognizable organ is the foetal brain. In fact, just after 30 days, the single-celled fertilized egg develops into an embryo with the shape of capital 'C'. At the top of this C-shaped structure, there are three small bumps, which are the starting tissues of the forebrain, mid brain and hind brain, while the rest of the C-shaped structure is the beginning of spinal

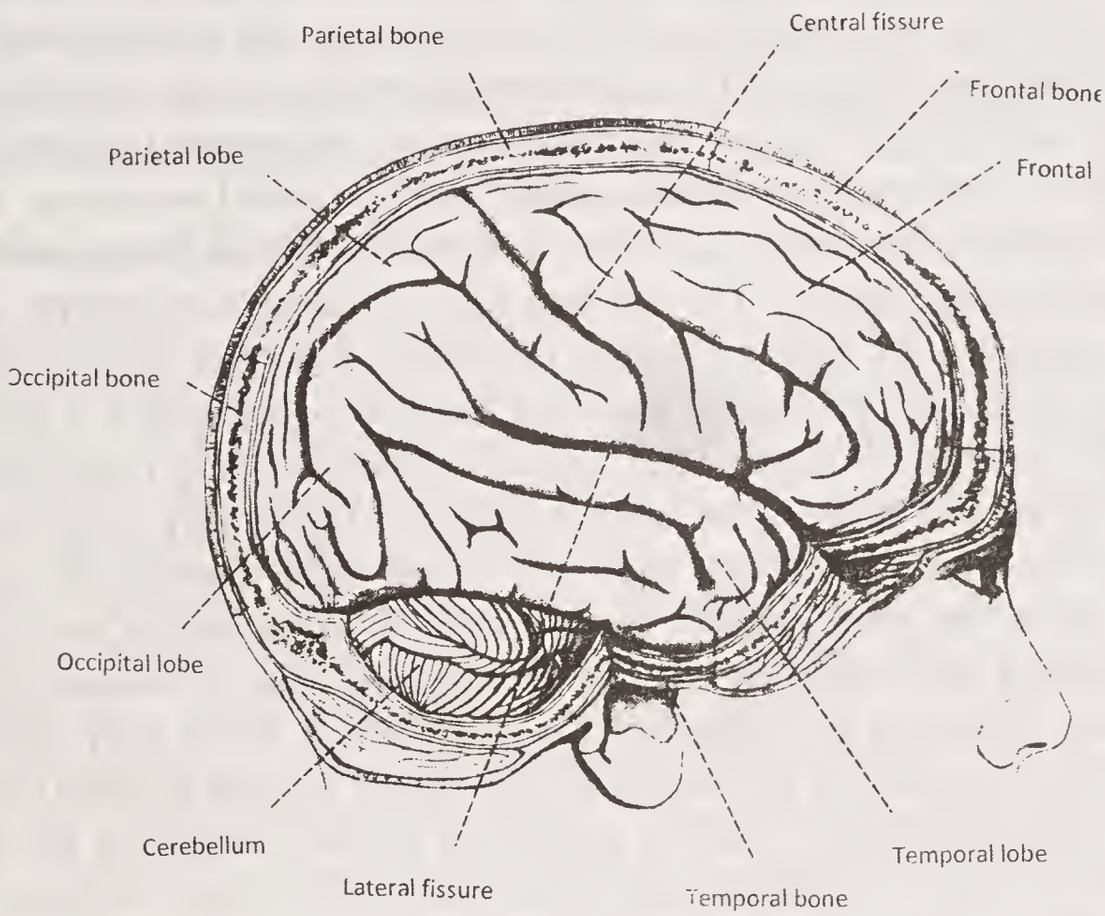
cord. At birth a baby's head is about a quarter of its body size. In fact, a newborn baby has over 100 billion neurons, which are much in excess than what are actually present in the adult brain. Brain development in a baby is very fast as the brain reaches between 75 and 80 per cent of adult size within the first two years. By age two, synaptic density is, therefore, observed to be at its maximum.

Peter Huttenlocher of the University of Chicago has shown that the postnatal period is very crucial as during this period, rapid neural interconnections and formation of synaptic junctions occur in human frontal cortex. Actually, a large variety and number of new connections are present in early embryonic life, from which the brain selects the most useful neural connections. It is this selection process that fine-tunes the neural network, which is by simply eliminating, through a weeding-out process, the less useful neural connections. This prunes the wiring in the brain leaving only those neural connections that are needed to interact successfully with the environment. This explains why the developing, immature brain has striking plasticity, clearly reflected in the ability to learn new skills early in life that become exceedingly difficult to learn as an adult. No doubt, toddlers are tireless explorers! Further, from about age 3 to 11, a child's brain has a much higher rate of metabolism. This means that it utilizes more energy that is indicative of higher brain building activity. Recovery from tissue injury in the brain is also faster in early childhood as a child's brain has a higher capacity to reorganize itself due to the presence of surplus neurons and synaptic junctions.

Functions of the Human Brain

Our problem-solving abilities depend mainly on a part of the brain called the cerebrum, which is divided into two parts called the left and right cerebral hemispheres. These hemispheres are formed by the division of the cerebral cortex by a longitudinal fissure that is a deep grove that runs down the centre of the brain front to back. There are other grooves that divide the surface of each hemisphere neatly into four parts called lobes: frontal lobes, temporal lobes,

parietal lobes and occipital lobes. The temporal lobes, named so because of their location at the temples, analyze much of the auditory inputs from the environment and are involved in memory, while the occipital and parietal lobes (in the rear and upper regions respectively) provide information about where objects are. The frontal lobes in each hemisphere play a vital role in thinking and planning of actions.



The human brain as it sits inside the skull

The left and right hemispheres have different functions and specialties. The left hemisphere is important for all forms of communication and is responsible for 'logical' thinking, speech, written language, number skills and understanding scientific concepts. We know this because when the left hemisphere is damaged, perhaps as a result of an accident or a stroke, there can be serious problems in speaking. The left hemisphere specializes in controlling certain movements, which include the movements we use to communicate. Studies by the Frenchman Paul Broca have

revealed that a piece of the left frontal lobe works as a centre for producing speech. Further, a German neurologist named Karl Wernicke discovered an area on the left temporal lobe, near to the Broca's area, that was a centre for understanding speech. There certainly occurs an interdependence of different lobe functions that helps to coordinate various brain activities.

The right hemisphere, on the other hand, specializes in receiving and analyzing information from the outside world. Therefore, damage to the right hemisphere may result in difficulty in identifying a face or any other sensory perception received by the five sense organs which connect us to the world around us. The right half of the brain is involved in 'creative' thinking, imagination and artistic insight. The left and right cerebral hemispheres are connected by fibres running crosswise between them called commissures. The largest and most important commissure is called the 'corpus callosum'. The commissures are useful in exchanging information between the two hemispheres. That is why the left half of the brain controls the right side of the body whereas the right half of the brain controls the left side. As most people are right handed, their left brain takes control and is dominant because logic and reasoning are important for our survival today than simply being imaginative and having artistic talents, as even schools focus mostly on subjects such as maths and science instead of art and music. Ideally, both the right brain and the left brain, working in unison, is the key to healthy brain activity.

Normally, the various systems of the body like digestion, blood circulation, breathing, reproduction, growth etc., occur involuntarily under the control of both nervous system and the endocrine system. The latter comprises various ductless glands — pineal, pituitary, hypothalamus, thyroid, parathyroid, thymus, pancreas, adrenals and gonads— that produce different chemical messages in the form of hormones, which travel through the circulating blood to reach particular tissues and alter the cellular functions. These basic life processes are controlled by the brain stem and the structures connected with it, namely the medulla and pons. The seat of emotion

in the brain happens to be the limbic system that comprises the top part of the brain stem and the region bordering the lower brain that is involved in instincts and inherent drives, and the higher brain areas that comprise the cerebral cortex. The structures namely, amygdala, hippocampus and hypothalamus are considered to be the parts of limbic system that are predominantly engaged in charging our lives with various emotions like love, hate, anger, greed, lust, envy etc. For example, persons with some damage in the limbic system, particularly the amygdala, show behavioural disorders as such persons typically show sudden outbursts of emotion on slightest provocation.

Male and Female Brains

Interestingly, sex hormones are necessary both for forming the genitals and for the behavioural and brain differences between the sexes. The hypothalamus, which is a tiny structure at the base of the brain, regulates many basic functions, such as eating, sleeping, temperature control, and reproduction. A specific part of the hypothalamus, responsible for sexual behaviour, is larger in male brains than in female brains, and also in human and non-human animals. Actually during embryonic development, the male hormone called testosterone is known to affect the action of certain brain chemicals in the male foetus. This perhaps predisposes men to react more strongly to stress and causes greater aggressiveness in them.

Although male and female brains largely function in the same way, there are subtle differences in their brains. For example, if the task is to define words, men appear to use only their left hemisphere, while women use both. The area of the anterior commissure seems to be larger in women, and some researchers have found that the back part of the corpus callosum is larger in women, and this could perhaps make the male and female brains work differently. Men are generally better at handling gadgets and have spatial-navigational skills like map reading and judging distances, whereas women have a better memory for words and objects, and have finer motor skills.

Experiments carried out on mice have shown that for development of parts of the brain which, in humans, are responsible for intelligence, mother's genes play the dominant role, whereas the parts of brain which control the basic instincts and influence the emotional make-up of an off-spring take proper shape due to the father's genes. Could this astonishing finding be true for humans as well? If so, women again would get the credit of endowing the human species with an intellect unparalleled in any other living organism. An interesting repercussion that this finding could have on our society is that men would look for smart and brainy wives for bearing intelligent offsprings! Although there is no direct evidence that this finding is true in humans, genes which carry a tag of their parental origin have been discovered in human beings.

Normally, all genetic traits of an individual, be they defining the colour of eyes or the texture of hair, are controlled by pairs of genes. Of the two genes responsible for a particular characteristic, one comes from the father and the other from the mother. The one which is dominant becomes active. However, a different set of genes called 'imprinted' genes, are active only if they happen to be inherited from a particular parent. So, the genetic information buried in these genes is decoded in the form of proteins – the vital, functional molecules to run the cellular machinery, only if they are inherited from the right parent. Experiments in mouse embryos have shown that imprinted genes descending from the mother are vital for early development of an embryo that includes the formation of neural connections, while those which came from the father are essential for development of tissues that provide the growing embryo nourishment, namely placenta.

Needless to say, the existing knowledge on the functional intricacies of the human brain is breathtaking. Understanding of the various aspects of brain evolution, as the human species evolved through the ages, clearly sheds light on the fact that human beings enjoy superiority over all other life forms only because the human brain is endowed with astounding abilities that are unique to our species.

2

The Making of Neural Networks

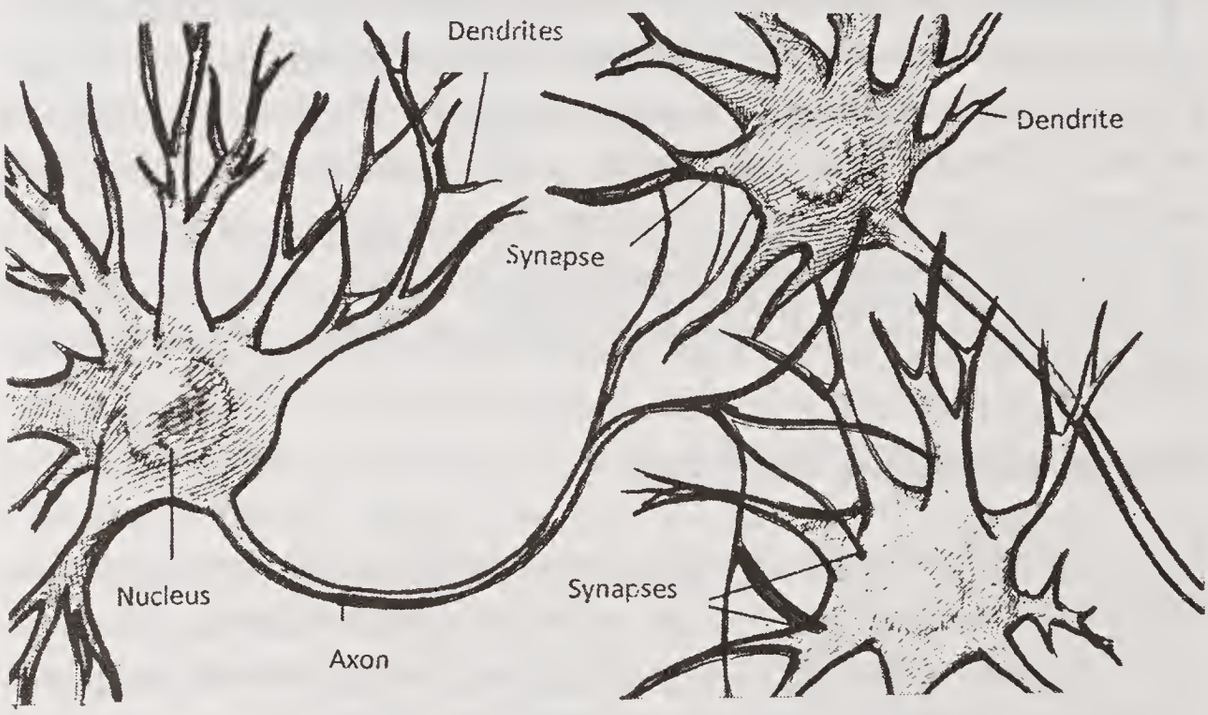
Just as any information flow is facilitated by proper connections between the sender and receiver, the flow of information to and from the brain is through a complex network of nerves that connect brain to all body parts. However, a still more complex neuronal network exists in the brain itself by which, billions of nerve cells are connected to each other forming an infinitely complex network of nerve processes that ultimately carry out the innumerable brain functions.

The Neuronal 'Chit Chat'

In a neuronal network, a single nerve cell could be connected to thousands of neighbouring nerve cells. Communication between cells of such complex biological circuits in the brain takes place through a chemical signal, the proper flow of which is essential for several brain functions. It is basically for their discoveries concerning this signal transmission between nerve cells that Arvid Carlson of the Department of Pharmacology, University of Gothenburg, Sweden; Paul Greengard of the Laboratory of Molecular and Cellular Science, Rockefeller University, New York and Eric Kandel of the Centre for Neurology & Behaviour, Columbia University, New York were jointly awarded the Nobel Prize in Physiology or Medicine for the year 2000. These pioneering discoveries concerning the chemical signaling between nerve cells are crucial for understanding the normal functioning of the brain.

Nerve cells or neurons have a central core or cell body containing a nucleus that carries the genetic material. Synthesis of

different proteins is directed by the nucleus,which act as signal molecules or *neurotransmitters* that travel from the cell body, in the form of an electrochemical signal, passing down the neuron at lightning speed, to a long process called axon which branches into thousands of nerve endings.This signal is then transmitted from the nerve endings to the slender protrusions or tentacle-like structures called *dendrites* sprouting from the cell body of connecting neurons, thus enabling one neuron to link with thousands of its counterparts.



The flow of chemical signals from one neuron to another could be likened to chit-chatting between those neurons

The site of contact between nerve endings of one neuron and dendrites of another is called the synapse, and it is at these synaptic junctions that several neurotransmitters carrying specific signals coded in their molecular structures are released.On being released at the nerve endings, the neurotransmitters bind to the receptor molecules present on the surface of dendrites of a receiving neuron, thus triggering another electrical impulse that carries on the message. Different neurons, therefore, 'chit chat' with each other in a language understood in the form of these chemical transmitters.

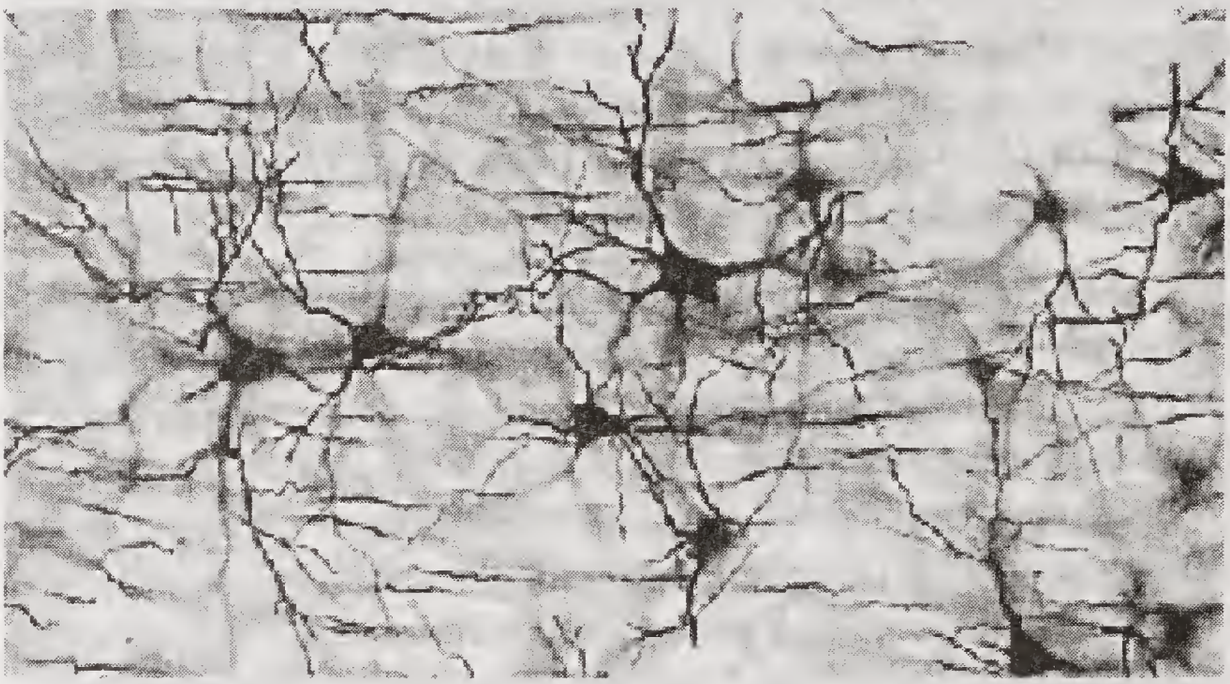
The credit for the discovery that the chemical 'dopamine' is a neurotransmitter, a key molecule in the brain responsible for

controlling body movements goes to Arvid Carlsson. His pioneering work, which he did about five decades ago, conclusively proved that dopamine is not a precursor of another neurotransmitter,as was believed earlier, but is itself a powerful transmitter of electrical signals between neurons. Carlsson actually developed an assay by which tissue levels of dopamine could be measured with high sensitivity. He found that dopamine was particularly present in the cluster of neurons forming a region called 'basal ganglia' in the brain. This part of the brain plays a phenomenal role in controlling motor behaviour or body movements.

Needless to say, abnormally low and high levels of dopamine give rise to many diseases. Carlsson showed that experimental animals treated with 'reserpine' (a naturally occurring substance that depletes neurotransmitters) lost their ability to perform spontaneous movements. But the breakthrough occurred when Carlsson treated these animals with 'levadopa' (L-dopa) — a chemical precursor of dopamine. Result: The animals regained their normal motor behaviour. Carlsson experiments showed that the persons suffering from Parkinsons disease or the 'shaking palsy' have a very low concentration of dopamine in the basal ganglia of their brains as neurons producing dopamine are degenerated. This causes difficulty in body movements and severe muscle rigidity marked by tremors. Carlson's research thus, conclusively established the role of dopamine in the brain. A direct impact of this discovery has been the development of an efficient remedy for Parkinsons disease. As the drug, L-dopa, gets transformed to dopamine in the brain, this chemical brings back the required levels of dopamine in the basal ganglion which, restores to quite an extent, normal muscle movements in Parkinson patients.

On the contrary, increased level of dopamine is the hallmark of the psychiatric disorder named schizophrenia. Based on Carlsson's research, anti-psychiatric drugs have been developed which act preferentially on the synaptic functions, blocking dopamine receptors on dendrites of neurons receiving the electrical impulses. Thus, the passage of 'unwanted electrical impulses is

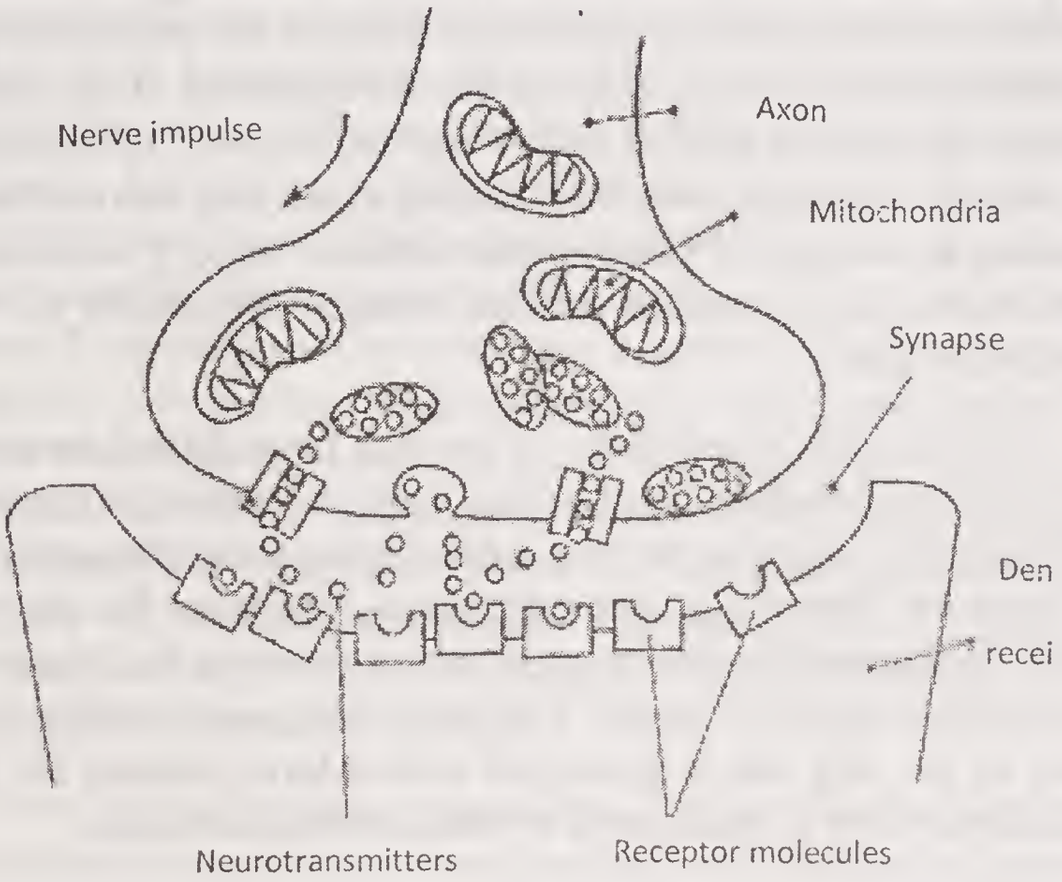
hampered. A new generation of anti-depressive drugs, which similarly block the receptor of another neurotransmitter namely, serotonin has been developed, thanks to Carlsson who discovered the importance of chemical signaling between nerve cells — the essence of all brain functions.



A complex network of neurons

Even though the existence of neurotransmitters in the brain was known, the precise mechanism of action at molecular level became clear only in 1960s through Paul Greengard who discovered the key chemical reaction that marks all communications between neurons. Called 'protein phosphorylation', this chemical reaction involves the addition of phosphate groups to a protein which rather dramatically changes the form and function of the altered protein. Greengard showed that when the dopamine produced by a neuron, binds to a receptor or an adjacent neuron, a cascade of reactions occur instantly. To start with, levels of messenger molecule, cyclic adenosine monophosphate (cAMP) rise which, in turn, activates the protein kinases. Activated protein kinases further add phosphate molecules to other proteins present in neurons. An important group of such proteins are the ones which constitutes the cell's gateways. Called the 'ion channels', such proteins are obviously located in the cell membrane allowing the entry and exit of only select

molecules in or out of the cell. As phosphate groups are added to an ion channel protein, it gets activated, thus allowing the entry and exit of certain ions. This causes the release of neurotransmitters.



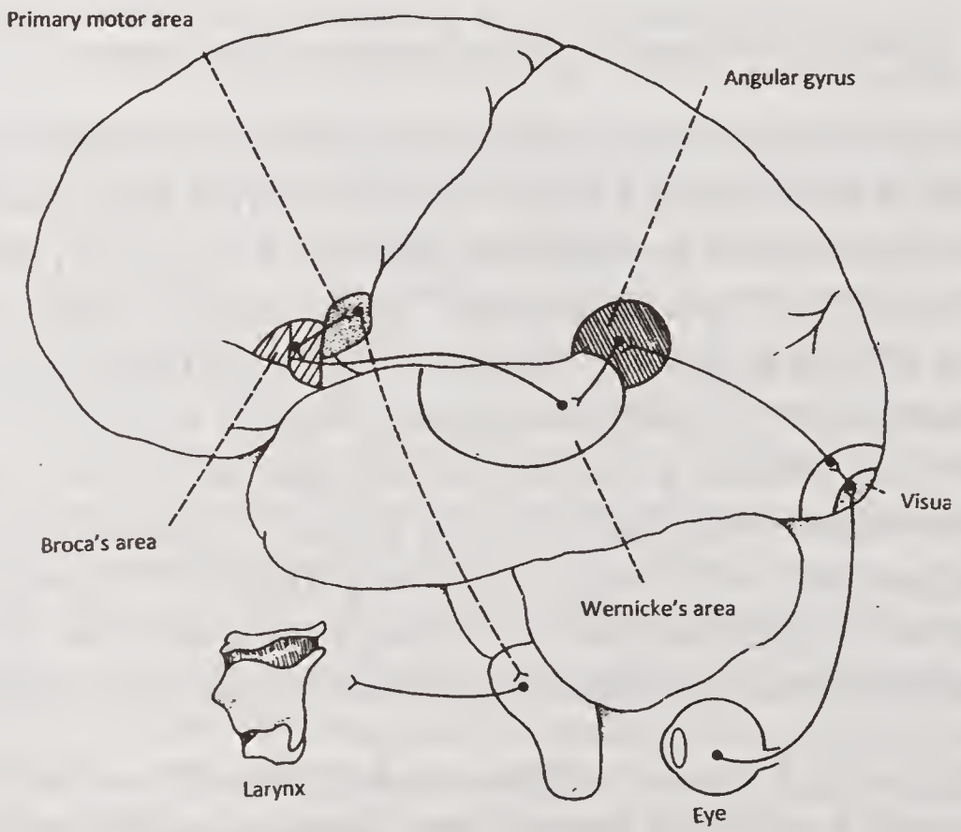
Close-up of a synapse—The meeting place of two neurons

Thus,Greengard showed that several neurotransmitters trigger a cascade of reactions in a neuron which involves the addition or removal of phosphate groups from proteins. A regulatory protein called DARPP-32 was discovered by Greengard which when activated, affects several ion channels of neurons, thus controlling the transmission of electrical signals through a synapse. The discovery of protein phosphorylation that influences signal transmission in neurons has ultimately helped in understanding the mechanism of action of many drugs.Phosphorylation of proteins is indeed a very significant event occurring in neurons. The work o Eric Kandel revealed its importance in the formation of memories

Basically, Kandel worked on Aplysia, the sea slug a experimental model and showed how changes in the shape an

function of a synapse in its neuronal network play a key role in the learning process and storing memories.A sea slug has neurons, many of which are quite large. A simple reflex of this animal that protects the gills was used by Kandel to study its basic learning mechanism. Certain external stimuli are known to enhance this protective gill withdrawal reflex of sea slug. As the strengthening of the reflex remains for several days, it shows that the sea slug 'remembers' the stimuli. Kandel showed that learning in sea slug was due to an increase in the size of synapse that connects sensory neurons to those motor neurons which activate muscles responsible for the protective reflex.

Such classic experiments in sea slug have further revealed that protein phosphorylation of ion channels present in synaptic junctions play an important role in developing short term memory. As these ion channels are phosphorylated, they allow the entry of more calcium ions into the neurons which enhances the release of neuro-transmitters at synapse. This molecular event actually took place in sea slug which developed a short-term memory for the protective reflex in response to a weak, external stimulus.



Nerve pathways involved in reading a sentence and reading it out loud

Kandel showed that a more powerful, long lasting stimulus is required for the formation of long-term memory in the sea slug. Deciphering the changes occurring at molecular level for developing long-term memory, Kandel showed that a strong external stimulus increases the levels of cAMP in neurons. This activates protein kinases which, in turn, trigger the activity of certain genes in the neurons. The two proteins encoded by these genes affect the shape of synapse. An increase in the size of a synaptic junction creates a long-lasting transmission of chemical signals between the connected neurons. Kandel also showed that if the synthesis of new protein is prevented, the long-term memory gets blocked but not the short-term memory. Repeating these experiments in mice, Kandel proved that the basic learning processes as studied in the sea slug were same in all mammals. As cellular and molecular mechanisms which make us learn and remember things are understood, there is a sure possibility of developing new drugs for enhancing memory power in patients who suffer from various types of dementia and memory loss, typical of Alzheimer's disease.

This award winning work has thus, helped us to understand how the human brain functions and performs the bewildering range of tasks assigned to it. It has provided the key to unraveling the changes in brain chemistry which gives rise to many neurological and psychiatric diseases.

Nitric Oxide as Signal Molecule

It is known that Nitric Oxide (NO) is not only generated by blood vessels cells but also by nerve cells. NO acts as a vital communicator and signal molecule in the human brain and other body parts. It basically acts as a neurotransmitter – a chemical signal which is passed on from one neuron to another. Neurons are indeed the most communicative cells in the body that are involved in the constant flow of information that takes place amongst them.The language of communication is of course chemical.

These chemical signals alter the interaction among the brain's neurons which ultimately control scellular chemistry and

orchestrates the working of various organs.Neurotransmitters are known to be of three types. The first type constitutes amines like acetylcholine, norepinephrine and serotonin. These are organic molecules whose nitrogen group mainly takes part in the signaling process. The second group includes some amino acids – the building blocks of proteins like glycine and glutamic acid or glutamate. Peptides like endorphins are third type of neurotransmitters, which are essentially small protein molecules. All these classic neurotransmitters are actually stored in small vesicles present within the nerve endings. Once released at the synapse, the neurotransmitters bind to specific receptor molecules present on the dendrites of the adjacent neurons.

The chemical message is thus passed on to another neuron and this neuronal signal transmission, is ultimately manifested in some action or thought process of our body. For example, low levels of serotonin in parts of the brain predisposes such individuals to act on suicidal thoughts.Similarly, norepinephrine flows through the brain stimulating adrenalin that is responsible for alertness in the body and helps in mental focus and muscle performance, while its low levels cause anxiety, lack of focus, and sleepiness. Phenylethylamine, which is also found in chocolate, gives us a feeling of bliss.Abnormal levels of neurotransmitters, either excessively high or abnormally low levels are infamous for the origin of several disorders.

Unlike other neurotransmitters, NO, which is a gas, cannot be stored in synaptic vesicles. In fact, it is so unstable that it gets converted to nitrate and nitrite within seconds. For the synthesis of NO an enzyme called NO synthase is present in the neurons which forms NO from the amino acid, arginine. Once released,NO passes out of the neuron's cell surface and comes in contact with adjacent neurons and simply diffuses into them.But exactly how NO takes part in the brain's activities is breathtaking.

Glutamate is the major neurotransmitter released in brain neurons. It acts by stimulating the formation of molecules called second messengers like cAMP.It is now clear that it is the presence

of the signaling molecule, NO, that enables glutamate to stimulate cAMP formation which further brings changes in the cellular machinery. Today, scientists have even deciphered, at molecular level, how glutamate stimulates NO formation in split seconds to convey signals from one neuron to another. When glutamate is released at synapse, it binds to its receptor molecule present on the dendrite of adjacent neuron. This binding opens up channels which allow the entry of calcium ions into the cell. Once inside the cell, calcium binds to a protein, calmodium, which is a crucial part of NO synthase and controls its enzymatic functioning.As NO synthase is turned on, NO is released.

Excessive release of glutamate may, however, damage neurons especially in cases of a stroke caused by blood clots in arteries of the brain. Drugs which block the glutamate receptor, or alternatively, inhibitors of NO-synthase markedly help in preventing nerve damage due to stroke. Nitroarginine, a potent inhibitor of NO synthase comes to the rescue of such patients. This is indeed a novel way of treating human stroke victims. NO is a vital neurotransmitter,in not just the brain's neurons but all nerve cells of the involuntary nervous system throughout the body. NO-releasing neurons have been found throughout the gastro-intestinal tract. The network of such neurons which regulates the entire process of digestion is called the myenteric plexus. These nerves regulate the contraction and relaxation of the muscular wall of intestines.

The role of NO as signaling molecule in the normal functioning of male penis is yet another striking finding. As NO regulates dilation of blood vessels in penis, the erection of penis occurs only when specific NO-releasing neurons become active. Based on this knowledge, new drugs against impotence are being developed. NO is also found to be released by macrophages – a type of white blood cells which are active in inflammation.These cells are a source of NO when the body is attacked by harmful substances. Macrophages then engulf and kill the invading foreign particles as well as tum or cells. Drugs which stimulate the function of NO synthase can, therefore, regulate the activity of macrophages.

As NO-releasing neurons are present throughout the body and regulate diverse biological activities, the therapeutic potential of drugs that stimulate or inhibit the formation of NO knows no boundaries. Harnessing the immense potential of this finding, pharmaceutical companies all over the world are working on developing drugs which can suitably manipulate the release of NO and rescue the human body from diverse forms of illnesses.Understandably, all this has stemmed from the Nobel Prize winning discovery that NO, a notorious air pollutant, is actually a good samaritan molecule which causes vital signaling in biological systems. An ironical fact, indeed!

The Memory of Sensations

The organs of sight, hearing, taste, smell and touch act as windows to the outside world as they keep the human body constantly connected with its environment, by picking up sensory signals which are rapidly processed in the human brain. The memory of select sensations sometimes last a lifetime. For example, we live in a world full of different odours ranging from deeply invigorating odours to the most disgusting ones.Can we ever forget the peculiar yet refreshing scent that fills the air just after it has rained on parched soil? The rich aroma and sight of mouth-watering foods is a pure bliss too, and so is the smell of our favourite perfume that instantly peps us up. On the other hand, the stench of putrefying garbage and bad mouth odours is nauseating.

Not just that. The human brain has the innate power to recognize and remember different odours, so much so that strange smells from age-old preserved items like pieces of cloth, books etc., can curiously bring instant flashes of incidents that occurred long ago, places visited years back, and people who have already died. How do these smells take us down the memory lane, and revive vivid pictures in our mind of moments that were long forgotten? How the brain sorts out different odours and transmits this information into sensory signals that, in turn, affect perception and memory is today known well, thanks to two American scientists — Richard Axel, a professor at Columbia University College of

Physicians and Surgeons, New York, and Linda B. Buck at the Fred Hutchinson Cancer Research Centre in Seattle – – who won the Nobel Prize in Physiology or Medicine for 2004 for unlocking the secrets of the working of olfactory system from the molecular level to the organization of concerned cells.

Actually, as soon as an odourous substance is inhaled through the nasal passage, it is detected by special neurons — the olfactory receptor cells — sitting in a small area in the upper part of the nasal epithelium.The olfactory epithelium contains about five million olfactory neurons, each of which has about 10 hair-like cilia which have on their surface special proteins called the odurant receptors. These cilia protrude into a thin bath of mucus that covers the olfactory neurons. The inhaled odourous chemical first binds to the olfactory receptors that activates the latter and triggers an electric signal which reaches the olfactory bulb in the brain via the nerve fibres. From the olfactory bulb, the odour signals are further relayed to the brain's higher cortex, which handles conscious thought processes, and to the limbic system, which generates emotional feelings.

Axel and Buck have discovered a large gene family, comprising some 1000 different genes that encode odorant receptors, the presence of which gives us the ability to discriminate about one lakh odours! They unravelled neural pathways that begin with say, a whiff of our favorite dish and end up with an uncontrollable response like salivation. Interestingly, numerous combinations of receptor inputs are generated from the few olfactory receptors expressed in the olfactory neurons that help in recognizing thousands of different odours. So although human beings have only about 350 functional olfactory receptors, we can easily distinguish thousands of odours by this mix-and-match system.

Brain Signals in Hunger Control

Controlling appetite is indeed a wonderful way of reducing body weight. Amphetamines help in doing so as they boost the activity of some neurotransmitters like dopamine and noradrenaline, which

have been linked with the intake of food as they lessen the hunger. However, use of amphetamines is highly restricted as they have mood creating properties and people may easily get addicted to them. A new generation of safer amphetamine-like drugs have been developed like dexfenfluramine.These drugs are not addictive and instead of suppressing the appetite, they create a feeling of having eaten well. But sadly, these appetite controlling drugs lead to depression and also pulmonary high blood pressure.

Another neurotransmitter called Neuropeptide Y (NPY) is well known to be important in food intake. It is produced in a part of the brain called the hypothalamus. Administration of NPY in laboratory animals increases their food intake leading to obesity. Scientists are working to develop drugs which could switch off the NPY appetite signals in the brain, thus reducing the food intake in humans.Nevertheless, indiscriminate and over-use of slimming drugs should be strictly avoided.Casual dieters who simply want to slip into clothes they wore in their teens must be particularly cautious as health risks of taking these drugs far outnumber their cosmetic benefits. All that is needed is a readjustment of lifestyle, which means to eat wisely while doing regular exercise and the key to this surely lies in our own hands.

The neuronal wiring that occurs in our brains is unique in us all. Different brain circuits are known to play a specific role that is reflected in the way each one of us think and act in different situations of our daily lives.The hallmark of such intricate neuronal connections is indeed the passage of chemical signals through the wired neurons, signifying vibrant communication amongst them, which defines all our actions and thoughts that makes us what we are.

3

Brain Afflictions in the Young

Good health and illness are both part and parcel of our life. We all fall prey to numerous illnesses during the course of our lifetime, many of which are easily conquerable while others are bothersome as complete recovery is slow and some stay on with us as a life-long burden. Afflictions of the brain that raise their ugly head right from the early childhood indeed pose a very tough challenge for both the young victim who is oblivious of the impact of that brain deficiency on daily life and the parents, for whom managing the everyday needs of their affected child is exceedingly distressing and painful.

Prenatal stress is a crucial environmental factor that causes autism

Various childhood afflictions of the human brain like autism, cerebral palsy, dyslexia, Attention Deficit Hyperactivity Disorder (ADHD) among others affect hundreds of thousands of children worldwide. Let us understand the striking symptoms, probable causes, diagnosis and management of some of the commonly occurring brain anomalies affecting children.

Autism

This neuro-developmental disorder first appears during early childhood as the symptoms of lack of response to social stimuli become markedly visible. There are impairments in social interaction and communication as most autistic children do not develop proper natural speech. The victim has restricted interests like playing a single game and suffers from frequent loneliness and shows repetitive behaviour such as hand flapping, head rolling, or body rocking. They may show compulsive behaviour like arranging objects in stacks or lines. Studies have shown that such children may indulge in actions like hand biting or eye poking that may cause self injury. Parents of children with autism normally notice their child's unusual behaviour when the child is between two and three years of age, which is characterized by no babbling and gesturing by the child by 12 months no utterance of single words by 16 months and no two-word phrases at two years of age. For diagnosing autism, the available diagnostic instruments include a semi-structured parent interview, and secondly, observation and interaction with the child evaluating the cognitive, communication and other factors.

Brain imaging studies have shown that connectivity in brain circuits that support social behaviour are reduced in autism. As a result, victims of this disorder invariably show difficulties with communication and social interactions. Further, studies need to be done on searching the genes that shape the development of these circuits and how they become disrupted in this disorder.

Scientists have shown that the greatest decrease in neural connectivity occurs between a cluster of neurons involved in the

emotional aspects of social behaviour that is a part of the limbic brain. Parts of the brain that mediate emotional component of our social interactions, which make us understand the social rules about how other people behave and act, are present in the limbic region. Neural connectivity is similarly affected in the brain region involved in language and communication and that play a role between visual perception and movement.

Now what makes the brain to err? It is well known that autism has a strong genetic basis although environment also plays a significant role in its development. A large number of autistic individuals with unaffected family members have shown spontaneous alterations in their genetic material— Deoxyribose Nucleic Acid (DNA) due to deletions or duplication of small stretches of this blueprint of life.

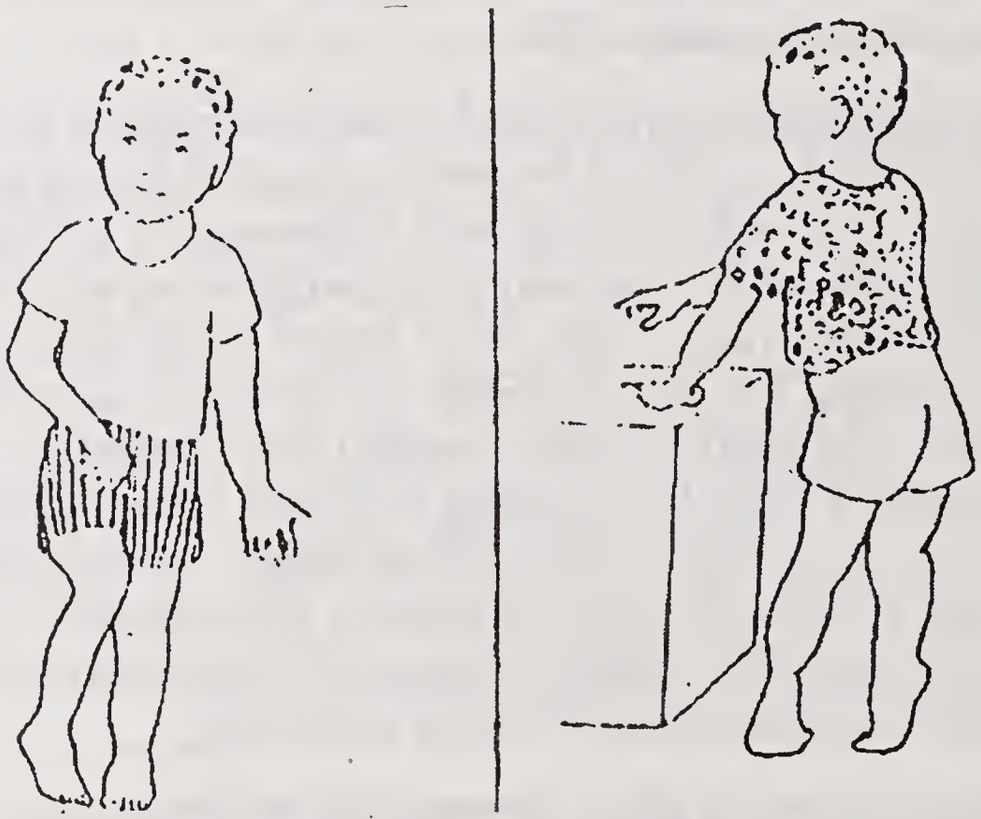
Research studies have pointed to the occurrence of synaptic dysfunctions in autism. It is at the synaptic junctions that one neuron meets the other and connects with it through the passage of neurotransmitters – the chemical signals that allow communication channels between two neurons, which defines neural connectivity in brain circuits. The most important environmental factor that is believed to contribute to autism is 'prenatal stress' caused primarily due to intake of alcohol and smoking by mother during pregnancy, exposure of the mother to certain drugs mainly anti-depressants, nutritional deficiencies in early pregnancy, advanced age of either parent, exposure of the mother to chemical pollutants and infectious agents and complications at or shortly after birth.

Basically, autism affects the amygdala, cerebellum and many other parts of the brain. Scientists believe that this brain anomaly takes root soon after conception and from there starts a cascade of events in the brain that are influenced by environmental factors. Although the brains of most autistic children tend to grow faster than usual after birth, there is slower growth in childhood. Several cellular and molecular factors are attributed for this abnormal early overgrowth. As interactions between the body's defence machinery and the nervous system also begin during early

embryonic life, any abnormal immune activity during this period of growth could affect brain development.

Cerebral Palsy

This brain disorder is characterized by physical disability caused due to fault in motor neurons of the developing brain that control body movements. The part of the brain that is mainly affected is 'cerebrum', and palsy refers to disorder of movement. However, all paralytic disorders are not cerebral palsy. This damage to the brain could occur during pregnancy, childbirth or after birth up to about age three. It is observed that about 40% of all children who develop cerebral palsy are those who were born prematurely. This affliction also occurs more often in multiple births.



A child affected with cerebral palsy

Victims of cerebral palsy show impairments of different body movements, based on which this disorder is classified into four types: spastic, ataxic, athetoid/dyskinetic and mixed. Spastic cerebral palsy is the most common type of this disorder, occurring in 80% of all cases. This neuromuscular mobility impairment has its root in the upper motor neuron lesion in the brain and the motor

cortex. This further impairs the ability of some nerve receptors in the spine to properly receive the neurotransmitter called Gamma Amino Butyric Acid (GABA). This affects the movement of muscles that receive signals by those damaged nerves.

Cerebral palsy is characterized by abnormal muscle tone and lack of coordination in body movements that result in involuntary facial gestures and unsteady gait in most victims. Speech and language disorders are also common in persons affected with cerebral palsy that is associated with mental retardation and hearing impairment. Depending on the severity of this affliction, the victims even show many joint deformities. Treatment is multi-dimensional as it may include various therapies like occupational therapy, physiotherapy, speech therapy, drugs to control seizures, alleviate pain, or relax muscle spasms besides surgery to correct the abnormalities related to dysfunctioning muscles.

Fragile X syndrome

This is a genetic disorder that results in a spectrum of intellectual

Victims of Fragile X syndrome have typical physical features

disabilities and is marked by physical characteristics like an elongated face, flat feet, large or protruding ears, low muscle tone and large testes in affected males. The victims show social anxiety marked by poor eye contact and extreme shyness resulting in poor social interaction. The fault lies in the blueprint of life as the length of a trinucleotide repeat sequence (CGG) is abnormal that affects the expression of a gene called 'Fragile X Mental Retardation gene' present on the X- chromosome.

In normal persons this gene contains 5-44 repeats of the CGG trinucleotide sequence, whereas victims of fragile X syndrome have over 200 repeats of this CGG codon. The protein expressed by 'Fragile X Mental Retardation gene' plays an important role in neural development. This disorder can be diagnosed by genetic testing that employs a special biotechnique called 'Polymerase Chain Reaction' (PCR) for determining the number of CGG repeats.

Prenatal testing for diagnosing fragile X syndrome can be done by employing the techniques namely, 'amniocentesis' and 'chorionic villus sampling'. This early diagnosis of fragile X syndrome in foetus growing in the womb can allow the would-be parents to take an informed decision to terminate the pregnancy if the unborn baby is affected. Women who are carriers of the abnormal CGG repeats can be also identified that further allows genetic counselling as there is 50% chance that carrier women may give birth to affected sons. Although there is no foolproof drug treatment, supportive management may involve speech therapy, occupational therapy, and personalized interventions to improve educational and behavioural needs.

Attention Deficit Hyperactivity Disorder (ADHD)

This common neuro-behavioural disorder makes the affected children face many difficulties at school and home as the victims find it really hard to pay attention or focus on a single thing as they get easily distracted and act without thinking. Abnormal behaviour is evident in the preschool years as such children show symptoms

of hyperactivity and inattentiveness besides having social phobia and anxiety.

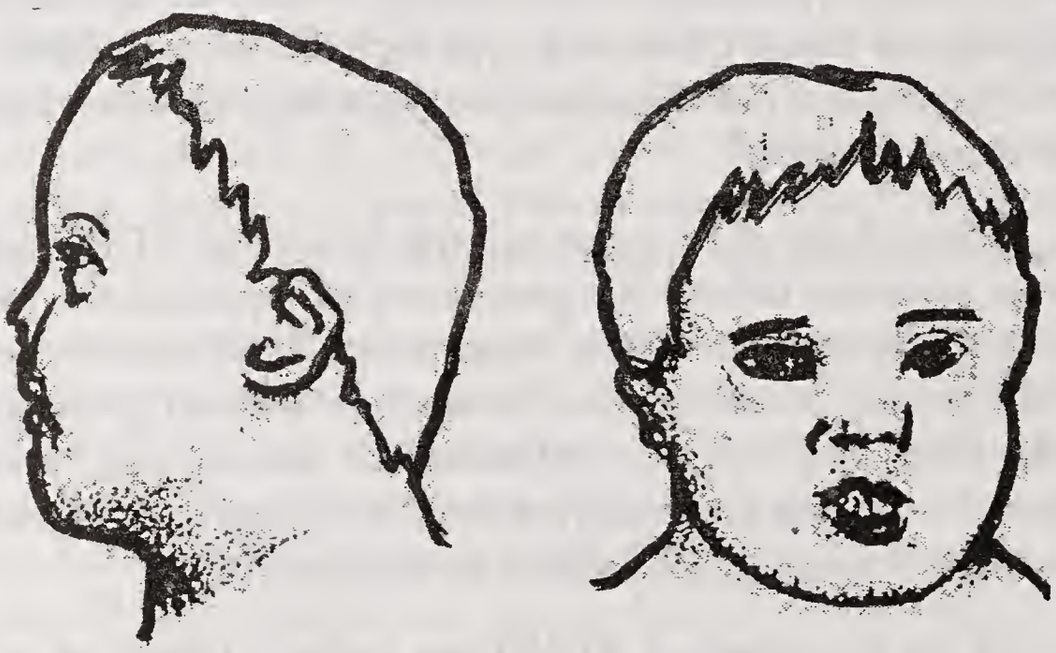
There are three different types of ADHD— Predominantly Inattentive Type includes those children who are unable to organize or finish a task and pay attention to details. They normally get easily distracted and find it difficult to accomplish routine daily tasks. Predominantly Hyperactive-Impulsive Type is diagnosed in children who talk excessively and find it hard to sit still for long. They feel extremely restless and act on impulse that is evident from actions like repeatedly interrupting others or speaking at inappropriate times. Combined Type includes those children who show symptoms of both the above two types, which severely impacts their learning ability.

Although the exact cause and risk factors for ADHD are not known, scientists believe that genes have an important role for this disorder to appear in children. Other possible factors may include brain injury and excessive use of alcohol and tobacco by the mother during pregnancy. Various viral infections like measles, varicella, rubella etc., during pregnancy, at birth, and in early childhood are also linked to an increased risk of developing ADHD.

As the symptoms of ADHD are similar to those of certain types of learning disabilities, clinical diagnosis of ADHD is not easy and it may be based largely on taking history of the child from parents and teachers. A combination of medicines, psychotherapeutic behavioural therapy, lifestyle changes, and counseling are a part of the treatment, which however, differs from child to child. Most cases, especially adolescents with ADHD, experience difficulties in social interaction and are at an increased risk of developing a substance abuse problem like misuse of alcohol and Cannabis. Victims of ADHD may also suffer from mood disorder and anxiety disorder. Research on children with ADHD has shown a general reduction of brain volume, with higher reduction of the left prefrontal cortex.

Down's Syndrome

This genetic disorder is also known as 'Trisomy 21', which is caused by the presence of all or part of a third copy of chromosome 21. It is estimated that chromosome 21 contains 200 to 250 genes. This most common chromosome abnormality in humans is associated with mental retardation and the victims have typical facial characteristics. As there is severe intellectual disability in such patients, pregnancies are often terminated if this disorder is detected in the growing fetus by prenatal screening.



A victim of Down's syndrome

Victims of Down's syndrome show a delay in motor skills and speech, and also have an increased risk for developing epilepsy and Alzheimer's disease. The occurrence of congenital heart disease and risk for dysfunction of thyroid gland (hypothyroidism) are also high in newborn babies with Down's syndrome. There are several deficiencies related to gastrointestinal functioning besides reduced fertility prominent in such individuals. Eye disorders are quite common in persons suffering from Down's syndrome, and particularly there are small white or greyish/brown spots on the periphery of the iris. Similarly, hearing impairments are also common in the victims. Notably, there is a high risk for a woman above age 45 of conceiving a baby with Down's syndrome.

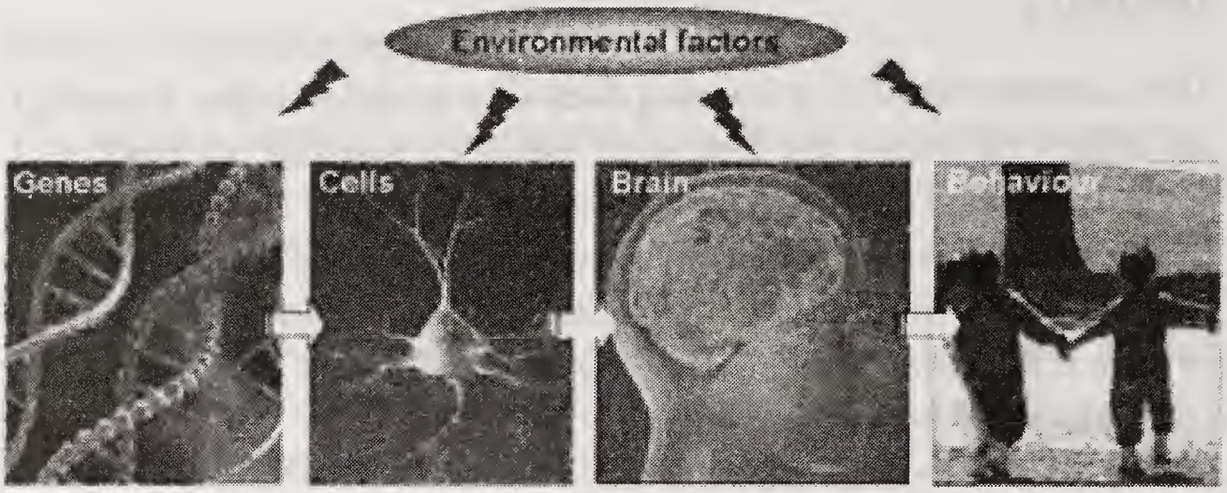
Dyslexia

This disorder signifies a learning disability in children that is marked by failure to attain the language skills of reading, writing, and spelling matching with their intellectual abilities. The severity of dyslexia could vary from mild to severe. The basic flaw lies in the brain's ability to translate images/sensations received by the eyes or ears into understandable language. However, it does not result from vision or hearing problems.

In most cases, dyslexia goes undetected in the early grades of schooling. As the child begins to get more and more frustrated by the difficulty in learning to read or write, he/she may further suffer from depression, low self-esteem and have problems with peer and sibling interactions. This may soon translate into child's dislike for school and other distressing behavioural problems.

There are several types of Dyslexia. 'Trauma Dyslexia' occurs after some form of brain trauma or injury to the area of the brain that controls reading and writing. Another type is called 'Primary Dyslexia' where the dysfunction occurs in cerebral cortex of the left side of the brain. Such children normally struggle with reading, spelling, and writing in Primary school years. Occurring more often in boys, 'Primary Dyslexia' is believed to have a genetic basis as it runs in families. A third type of dyslexia is known as 'Secondary or Developmental Dyslexia' where hormones are supposed to play a role in early foetal development. The severity of this form, however, reduces as the child grows up.

In general, dyslexia may affect several different functions, such as 'visual dyslexia' where there is number and letter reversals and the inability to write symbols in the correct sequence; and 'auditory dyslexia' that involves difficulty with sounds of letters or groups of letters as they are perceived to be jumbled or not heard correctly. A clinical psychologist may help in diagnosing this disorder by reviewing how the child processes information from seeing, hearing, and participating in various activities.



Both genes and environment have a role in triggering brain disorders in children

The interplay of genes and environmental factors is crucial for the development of most brain afflictions in the young. Genetic counselling can play an important role for couples, planning to have a baby, who have a victim of brain disorder in their families as with early prenatal testing the would-be parents can timely decide the abortion of the affected foetus. Moreover, for saving precious lives from such devastating illnesses marked by deficiencies in the organ that defines our superiority over other living beings, it is pertinent for pregnant women to take nutritious diet, and more importantly, they must stay away from stress, alcohol and tobacco!

4

Faulty Neural Circuits in Adult Brain

A host of brain disorders that raise their ugly head in adults are known to ravage lives of scores of people worldwide. The functional errors in neural networks of adult brain are known to cause disorders like Multiple Sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's Chorea and Epilepsy.

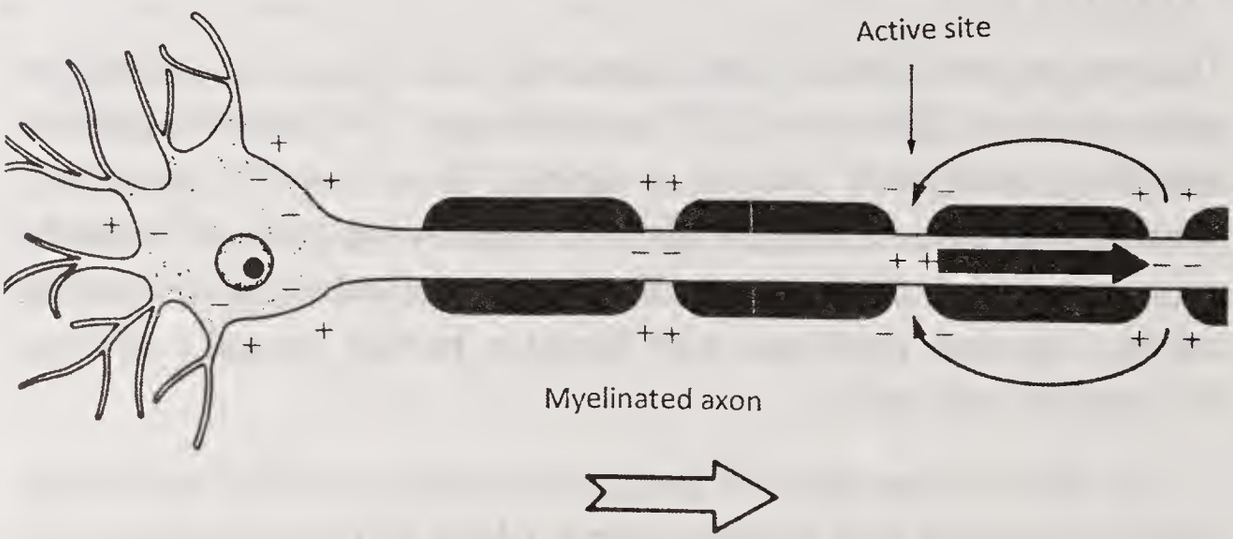
Multiple Sclerosis

This progressive disease of the central nervous system affects people in the prime of life between 15 and 40 years. The impending doom manifests itself with symptoms ranging from tingling sensation, numbness of parts of body, slight blurring of vision, slurred speech, muscle weakness, poor coordination, unusual fatigue, muscle cramps, spasms, problems with bladder, bowel, sexual functions to complete paralysis.

In this disease there is damage to myelin – a fatty substance which surrounds and protects nerve fibers in the same way that insulation protects electrical wires. When any part of this myelin is destroyed, nerve impulses to the brain are interrupted and distorted. This disease is believed to be caused by a virus that, in some way, is linked with the virus causing 'distemper', a common disease in dogs. This belief is based on several identical observations that an epidemic of distemper in dogs is usually followed by an epidemic of Multiple Sclerosis (MS) amongst the inhabitants of that region. This association of Multiple Sclerosis with the distemper virus has been further proved by the fact that many MS patients have had

contact with pet dogs for more that 10 years before contracting the disease. The symptoms however, develop any time between one to 20 years after contact with infected dogs. It is, therefore, wise to vaccinate dogs against distemper as a step towards prevention of this disability disease.

Another hypothesis qualifies Multiple Sclerosis to be an auto immune disease – one in which the body produces protective protein molecules called 'antibodies' against some of its own body constituents, unlike the normal state where the body's defence forces are alerted only to an unwelcome foreign invader. The immune machinery is affected in such a way whereby the otherwise trained immune cells find themselves incapable of distinguishing self from non-self. In essence, some unknown constituents of myelin are mistaken to be as foreign by the immune cells and consequently, are attacked by antibodies termed as 'auto- antibodies'.



The protective covering of neurons is damaged in multiple sclerosis. The picture shows electrical changes in a stimulated neuron.

Several efforts have been made in this direction to discover the constituents of myelin that apparently pose as foreign to the body. One such scientific endeavour has been amply rewarded. The credit goes to a research team of the centre for Neuro-chemistry in Strasbourg, who in cooperation with a group of medical scientists, have discovered a molecule known as CSL (Cerebellar Soluble Lectin). Nearing a medical breakthrough, the team observed in more

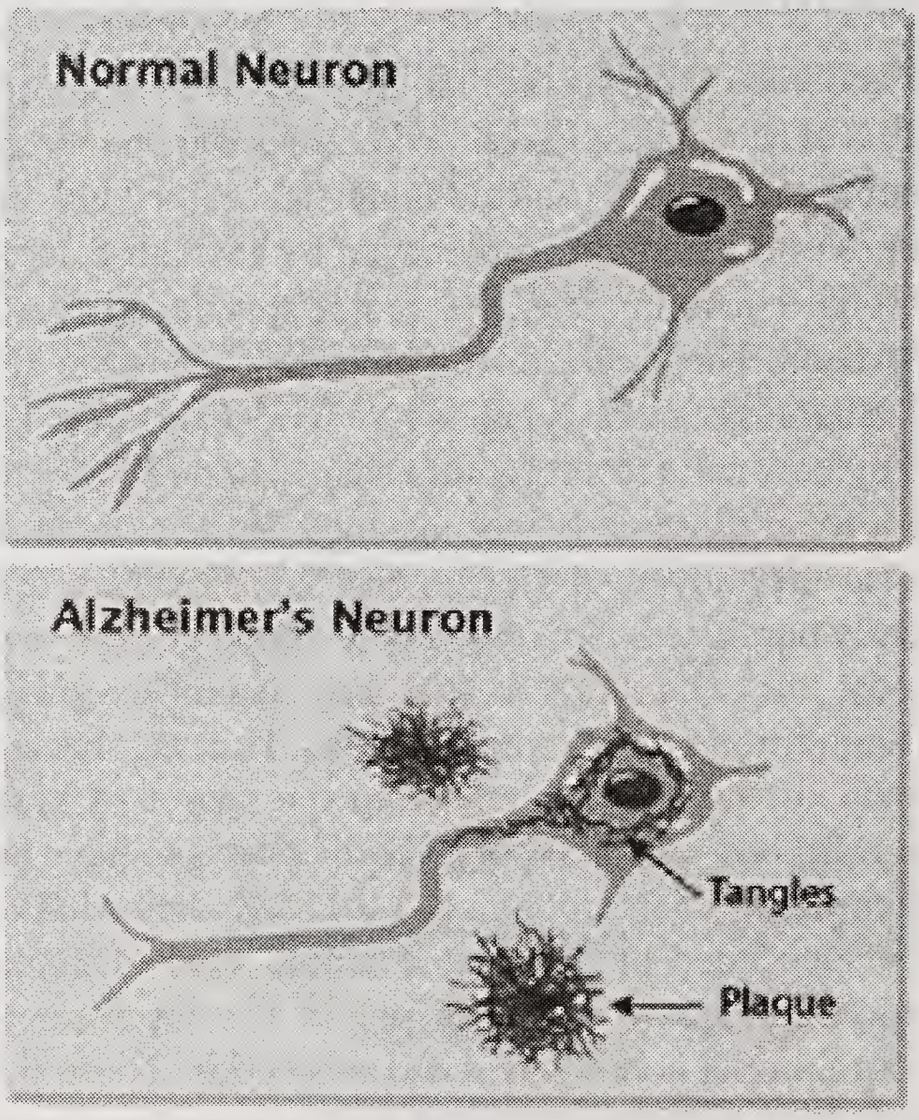
than 93 per cent of cases the presence of antibodies directed against this particular molecule in the cerebral fluid of patients suffering from Multiple Sclerosis. This discovery has also been used to develop a simple, rapid biological test that allows early diagnosis of Multiple Sclerosis.

For understanding the mechanisms involved in the origin and the progress of Multiple Sclerosis, technologies are important which could enable brain cells to grow under laboratory conditions. In most tissues of the body, cells damaged by any cause are replaced by new cells. Unfortunately, this is not so with the cells of the nervous system. These cells do not have the capacity to divide and multiply. Therefore, cells dying due to disease or injury cannot be replaced by new cells resulting into suspension of body functions dependent upon those cells. For instance, if the cells in the brain that control the movements of an arm are damaged, the arm is permanently paralyzed. Not only do the brain cells fail to multiply in the body, but even worse is that they cannot be grown under artificial conditions, of a culture media. This has been a major impediment in the way of unfolding the secret of brain cells. Astonishingly, however, this tough battle seems to have been won by the scientists in Johns Hopkins School of Medicine in Baltimore, who have succeeded in isolating a certain kind of human brain cells which can grow and multiply in the laboratory, under conditions of proper nourishment and cultivation. These significant discoveries, have given an optimistic shade to the future endeavours that may lead to new approaches to the cure of Multiple Sclerosis and other related diseases of the central nervous system.

Alzheimer's Disease

The greying of hair, the slow but steady appearance of ugly wrinkles all over the body, one by one loss of all teeth and decline of general vigour and exuberance of the bygone days, are not the only horrifying signals of advancing age, for a chronic dementing illness may also raise its ugly head as one grows older. Throughout the world, about 10 per cent of the people in their 70s and 40 per cent

in their 80s suffer from a progressive deterioration of intellect, memory and thought, popularly known as Alzheimer's Disease (AD). It is named after a German doctor, Alois Alzheimer who first described this disease in 1907.



Nerve cells get tangled in Alzheimer's disease

A major public health problem, AD deprives its victims of cognitive abilities. The distressing nature of this disease is reflected in memory loss that makes even day-to-day skills like tying shoelaces, pouring tea or buttoning a shirt very difficult for its victims. As the victim drifts away from performing the normal basic personal needs, the disease affects adversely his personality and social behaviour. It then shows up as a major psychiatric disorder. At this terminal stage, the patient becomes mute, beset with several neurological abnormalities such as seizures and is completely bed-ridden.

The onset of AD is so gradual that doctors miss it at its early stages. The disease becomes apparent only when mental derangement becomes marked and the person's behaviour turns to abnormal. It can only be diagnosed at early stages after examination of the brain tissue. More recently, however, advances in medical technology have given birth to new imaging techniques such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET), which permit visualization of changes in the brain structure making early diagnosis easier.

Shaking the earlier belief that AD is due to hardening of blood vessels or haemorrhages in the brain, Alois Alzheimer showed two characteristic lesions, clearly visible, in the brain of persons who died of this disease. Spread diffusely throughout the cerebral cortex and hippocampus regions of the brain of Alzheimer's victims are present small spherical structures known as 'senile plaques' and minute bundles of abnormal thread-like protein material called Neurofibrillary Tangles (NFTs). The plaques have a central core made of protein called beta-amyloid which is surrounded by degenerating nerve cells. The amyloid protein is fibril-like in nature. Although research studies have suggested that this protein is formed even in the normal, healthy brain cells, it is still unclear as to why it gets deposited as senile plaques in the brains of Alzheimer's victims and not in normal persons.

Beta-amyloid is a small protein containing just 42 amino acids, the building blocks of a protein molecule. It is, however, made from a larger molecule, the Amyloid Precursor Protein (APP). The latter, apparently, does not harm the cells as it is found even in normal brain cells. The problem arises only when beta-amyloid is clipped out of APP by some protein-splitting enzymes. But, in principle, this should not happen as APP is embedded in the cell membrane with only about two-thirds of beta-amyloid segment jutting out on the cell's exterior while the rest remains buried in the cell membrane, thus escaping the effect of protein-splitting enzymes. Normally, in healthy individuals, the outer APP segment is clipped off from the membrane and secreted out of the cell. In

other words, the cell is not able to produce beta-amyloid. In the unfortunate victims of Alzhiemer's Disease, a biochemical reaction occurs which makes possible the production of beta-amyloid protein.

The biochemical anamoly that leads to the production of beta-amyloid has been discovered. This finding suggests that cells have alternative ways of breaking down APP which may yield intact beta-amyloid fragments. This actually occurs in small vesicles of the cells called lysosomes, which are loaded with enzymes capable of cleaving just any bond in a protein. But why should the normal pathway of degradation of APP shift to such alternative pathways? One plausible reason is the presence of some inherent defect in APP . The puzzle was solved in 1991 when John Hardy, a neurogeneticist at St. Mary's Hospital Medical School, London, reported that a genetic alteration or a mutation occurs in the gene encoding APP. This gene has been traced to a location on chromosome 21. Interestingly, victims of a genetic disorder called Down's Syndrome who have an extra chromosome 21, usually develop beta-amyloid deposits in the brain cells and exhibit dementia similar to AD. The mutation in APP gene seems to predispose its carriers to AD. This is evident because in several families AD is inherited by one generation from the other. Whether it is a single gene that mutates or a whole lot of genes cause AD is yet not clear. Besides, influence of environmental factors are also not discounted. The defect may even lie in the enzyme that splits the APP during its normal processing.

The second prominent changes seen in the brains of Alzheimer's victims is the presence of NFTs, the rope-like filaments comprising two fibres twisted about each other. Though common in many diseases of the brain, NFTs are completely absent in healthy brains. These tangles severely inhibit the passage of nerve impulses from one brain cell to the other. This occurs due to destruction of synapses, the special connections between two nerve cells where one neuron ends and joins hands with the other forming a chain. Many such connections give rise to a neural network that is central

to many brain functions, including memory and thought process. The neural message that is transmitted from one nerve cell to the other is actually facilitated by a chemical compound called neurotransmitter.

Normally, a protein named 'Tau' forms a complex network, the cytoskeleton, in the cytoplasm of nerve cells and coordinates the movements of various molecules within it. If the cytoskeleton is disrupted, the cellular transport fails. In AD, the tau-protein is not the same as normal brain cells. It is modified with additional phosphate molecules tagged to it. The alteration in the structure of tau destroys its ability to form the assembly of the cytoskeleton. It eventually robs the brain cells of the 'highways' which are indispensable for ferrying the neurotransmitters and many other protein molecules to and fro the nerve cells through synaptic connections. As a result, the neurochemicals get piled up in the brain cells. Moreover, NFTs also deplete acetylcholine and norepinephrine that play an important role in communication between the nerve cells. All these contribute to the development of abnormal physiological changes.

Scientists even believe that certain neurotoxic substances present in plants may have a hand in leading the brain to such devastation. The exposure to these neurotoxins early in life may be damaging the brain which becomes visible only after many decades. Reports of high levels of aluminium in the brain cells of Alzheimer patients have intrigued scientists as to whether this element is the cause of the damage or just one of the products that appear as the disease advances. Another hypothesis on the cause of AD spawns from the fact that certain progressive diseases of the brain result from infectious agents such as a virus. Besides, there is also a speculation that chronic activity of body's defence machinery, such as in repeated infections, could lead to brain damage. All these put together suggest that the disordered chemistry of the brain cells in AD is due to complex interaction of several factors, as no definitive cause has yet been unearthed.

Meanwhile, efforts are in full swing for tackling the symptoms

of AD, namely, depression, agitation and psychotic behavior. However, the need of the hour is to devise a therapeutic strategy that could block the biochemical events associated with the formation of senile plaques and NFTs – the visible lesions – in the brain cells. Drug which can enhance the production of neurotransmitters, such as acetylcholine are being tested for their suitability in treating the disease. One such candidate drug, physostigmine, is very promising. Studies have shown that long-term administration of this chemical slows down brain damage. Yet another rationale suggests transplantation of active brain tissue taken from aborted human foetuses. This is thought to promote the regeneration of nerves and revival of the brain's functions in such patients. The practicality of this surgical therapy is rather doubtful since wide regions of the brain are affected in AD.

Another novel cure for this mysterious brain degeneration has stemmed up from a theory put forth by Joe Rogers of Sun Health Research Institute, Arizona, and Pat McGeer of the University of British Columbia, Vancouver. The duo emphatically advocate the use of anti-inflammatory drugs related to common aspirin for treating dementia associated with AD. Rogers and Geer believe that AD is essentially an inflammatory condition very much akin to rheumatoid arthritis –an excruciating disease where a severe inflammation of the joints occurs. "The neurological damage is caused by a locally overreacting immune system in which biochemical and cellular defense mechanisms turn against the brain cells they are meant to defend," say the researchers. What's more, the clinical trials with an anti- inflammatory drug named indomethacin have been quite promising.

Rogers and Geer suggest the involvement of beta-amyloid in the 'complement cascade'. Complement cascade is a chain of molecular events producing special proteins which can be fatal to foreign cells. It is triggered when the defense machinery of the body produces protective protein molecules called antibodies to counter the attack of foreign proteins known as antigens. Rogers and Geer seem to be on the right track since various other studies

have revealed that amyloid indeed has a 'short-circulating' effect. That is, it stimulates this cascade without any antibodies. This eventually causes the slaughter of otherwise healthy brain cells.

Scientists have further discovered that the brain lesions found in Alzheimer's patients are filled with a special type of cells called microglial cells. These cells in a normal brain function like 'house-keepers', disposing dead or wounded nerve cells. But they play a totally different role in Alzheimer's victims. Not only are they unusually ferocious in devouring the nerve cells but also appear to be secreting toxic protein molecules which belong to the complement cascade. Running amck, these cells do not even spare the innocent bystanders. To confirm their finding that AD occurs due to an overenthusiastic defense response against the nerve cells triggered by beta-amyloid, researchers have surveyed the hospital records of about 12,000 patients in USA and Canada who suffered from AD or rheumatoid arthritis. Only a small number of these had both the diseases, suggesting a link between susceptibility to arthritis and resistance to AD. This is so because most patients of arthritis take a lot of anti-inflammatory drugs and hence develop resistance to AD.

In yet another exciting study, Mc Geer along with a group of Japanese scientists has shown that the rate of development of dementia is very low in people suffering from 'leprosy'—a bacterial disease that specifically affects the nerve cells. This was particularly seen in patients taking 'dapsone', the drug of choice used to treat leprosy and a well known antibiotic having a powerful anti-inflammatory effect. The incidence of dementia was found to be as low as 2.9 per cent in patients taking dapsone compared to 6.25 per cent in those who did not take the drug. Interestingly, the senile lesions that appear in Alzheimer's patients were found to be conspicuously lacking in the leper brains.

A new avenue of research on AD is wide open. Search is on for better anti-inflammatory drugs which can penetrate the blood-brain barrier and cool the immunological fire, without having any

side effects. Drugs capable of blocking the production of beta-amyloid are other contenders for providing relief to victims of AD. Meanwhile, in a breathtaking finding, a team of scientists from Duke University led by Allen Roses could lay its hands on the very segment of the life's 'blueprint' that ultimately decides the fate of the brain cells of a person. They have shown that two versions of a gene called Apo-E2 and Apo-E3 protect people from developing AD but another form of the same gene, namely, Apo-E4 almost always causes the disease in its carriers by the age of 80. This spectacular development thus opened the way for designing drugs which could effectively block the activity of the 'bad' gene, thus making the impossible possible! This is a glimmering light in otherwise a dark alley of AD.

Parkinson's disease

Affecting neurons in the mid-brain that control body movement, this disease shows its ugly head with signs of weakness or stiffness in a limb or a trembling sensation in a hand when it is at rest. As the disease progresses, the shaking worsens and the muscles become more stiff leading to body's imbalance. This makes the patients incapable of doing day-to-day tasks, as the tremors or shakiness limits the ability to even stand or walk. Depression and other mental or emotional problems are also common in the victims.

Parkinson's disease is more common in men and it normally affects individuals in the age group 50-65 years. The part of mid-brain called the 'basal ganglia' is affected, whose cells require a proper balance of two neurotransmitters called 'dopamine' and 'acetylcholine'. The specific area of this part of brain where deterioration of nerves occurs is called 'substantia nigra'. Actually the cells that produce dopamine begin to degenerate and this disturbs the balance of these two neurotransmitters. Basically, dopamine acts as a chemical messenger between the substantia nigra and another area of the brain called 'corpus striatum', and this communication is crucial for coordinating smooth and balanced muscle movement.

Although the exact reason for the occurence of this disease is not clear, it is known to have a genetic link. Scientists also believe that certain toxins may selectively destroy the specific neurons causing Parkinson's disease. Toxins that may be linked to Parkinson's include manganese, carbon monoxide, carbon disulfide and some pesticides. Certain drugs such as anti-psychotics used to treat severe paranoia and schizophrenia can also cause a person to experience symptoms that resemble Parkinson's disease.

Treatment normally includes drug therapy and/or surgery that reduces the symptoms. Besides, a diet rich in fruits and vegetables, high-fibre foods, fish, and omega-3 rich oils have a protective effect against Parkinson's disease.

Huntington's Chorea

It is a degenerative, age-onset disorder of the brain that results in loss of body's response to various sensations and total mental incapacitation. The disease appears late in life, only after child-bearing years. It is named after George Huntington, an American physician who first described the inherited nature of this disease.

Huntington's Chorea is a genetic disorder where a single copy of the defective gene inherited from either parent is sufficient to spell disaster. Individuals with two copies of the faulty gene show the same degree of illness. It is, therefore, an autosomal dominant disorder. The faulty, culprit gene causing this brain disorder was identified in 1983 by scientists led by James Gusella, a Harvard molecular geneticist. Further, a marker DNA sequence linked to the faulty gene in Huntington's chorea was identified by Gusella, based on which a diagnostic test was developed which is being used at the Massachusetts General Hospital in Boston and the John Hopkins Hospital in Baltimore.

In an interesting study Nancy Wexler, a psychologist at the Columbia University and President of the Hereditary Disease Foundation has traced the inheritance of this disease in the world's largest family of Huntingtons' victims composed of about 9000

members, at Lake Maracaibo, Venezuela. Residing on chromosome 4, the defective gene has been linked to a repeat sequence comprising three nucleotides namely, CAG (Cytosine-Adenine-Guanine). These nucleotides repeats are formed as a result of mutations that occur during DNA copying. The insertion of extra nucleotides increases the repeat number. However, a mínimum number of 36 CAG repeats is the threshold length supposed to cause the disease. This linked marker for the faulty gene acts like a flag for tracing the defect through successive generations of a family. Unfortunately, Wexler, one of the top researchers in this field too carries this ill-fated gene!

Epilepsy

The victims of this brain disorder have recurring seizures, which occur when a cluster of neurons in the brain send out wrong signals and disturbs the normal neuronal activity, resulting in violent muscle spasms. The affected person may even lose consciousness. The enhanced neuronal activity typical of epilepsy happens due to some abnormality in brain wiring that actually results in an imbalance of certain neurotransmitters. An important neurotransmitter that plays a role in epilepsy is Gamma-Aminobutyric Acid (GABA). Although most seizures do not cause brain damage, but repeated uncontrolled seizures may cause brain damage. Clearly, this disorder has a stigma attached to it that it is the cause of embarrassment and frustration for its victims.

The cause of epilepsy may be brain injury and abnormal brain development. Specific genes may have a role in the occurence of epilepsy. For example, several types of epilepsy have been linked to defective genes that express ion channel proteins, which are the 'gates' that control the flow of ions in and out of cells and thus regulate neuron signaling. Interestingly, many people with epilepsy have normal or above-average intelligence. Certain tests and brain scans such as Magnetic Resonance Imaging (MRI) or Computed Tomography (CT scan) are common diagnostic tests for epilepsy. Once detected, the occurence of seizures can be controlled with modern medicines and surgical techniques.

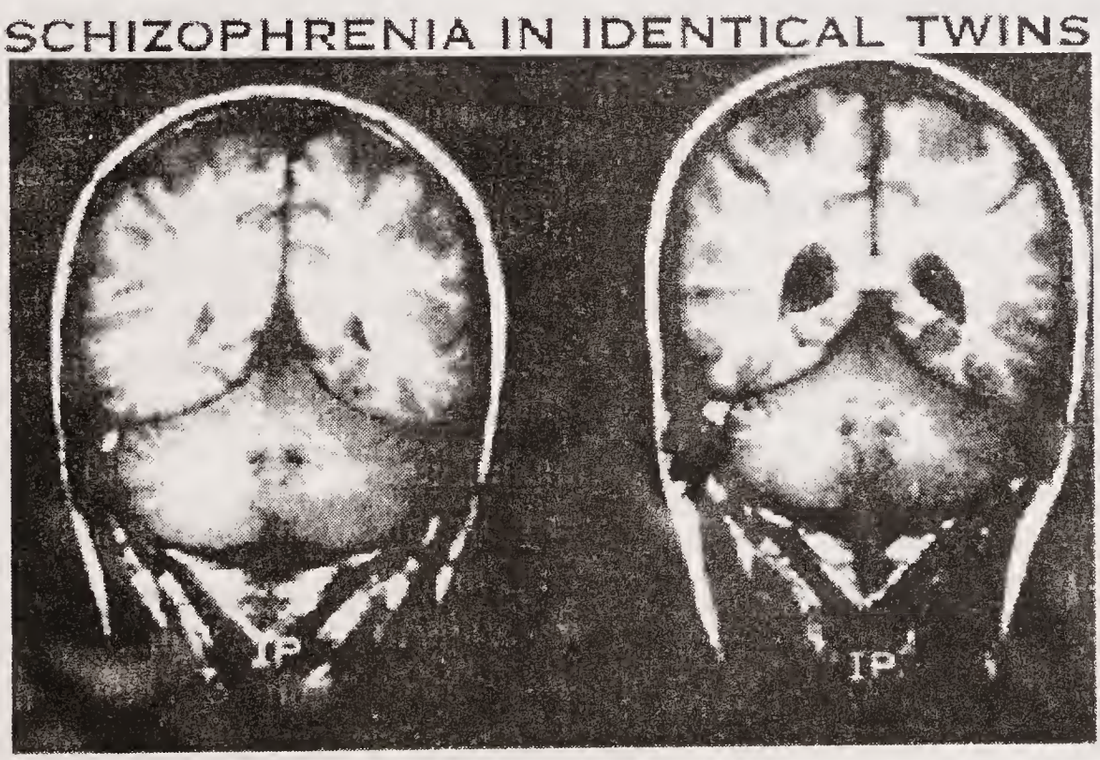
5

All in the Mind

Love works wonders. With no foolproof cure, the trauma of many psychiatric and psychosomatic disorders namely, Schizophrenia, bipolar affective disorder, manic depression, obsessive compulsive disorder and even drug addiction can be surely lessened through compassionate care and efforts to reintegrate the victims into society.

The Psychosis of Schizophrenia

Our actions make each one of us unique. Going a little deeper into what makes an action to occur, it dawns that every single action is



The MRI scan shows that the brain of a schizophrenic (right) is different from that of his healthy twin brother. Brain ventricles are enlarged in schizophrenia

preceded by a thought. Deeper still, it seems that thoughts arise due to physical sensations that stimulate the human body. Well, the human mind can also create sensations in the body through what we imagine, which in turn, may generate thoughts. Now what would happen if our mind is haunted by weird thoughts? Surely, our actions would then become weird and unacceptable to the so-called real world.

This exactly happens to the unfortunate victims of a mental disorder, popularly called Schizophrenia, who have a seriously disintegrated thought process. Affecting about one per cent of the human population, the thought process of the victim manifests itself as spine chilling paranoid or bizarre delusions and fearful auditory hallucinations. Responding to such delusional thoughts, the action outcome is in the form of disorganized speech and absurd behaviour with complete disconnection from the world we live in. Paul Valery has indeed rightly said that, "a man who is 'of sound mind' is one who keeps the inner madman under lock and key."

The Shocking Symptoms

It is deeply saddening that the onset of symptoms, typical of schizophrenia, occurs in young adults, commonly in the age group 16-32 years. Late adolescence and early adulthood are peak years for the onset of Schizophrenia, as these are the formative years critical to one's social and vocational development. Thus, what most parents might mistake as teenage problems could actually be the signs of a serious mental disorder, which is why immediate medical help is necessary. Normally, young adults who develop Schizophrenia experience non-specific symptoms like social withdrawal and general irritability before the actual symptoms of psychosis begin to show more prominently.

Commonly, schizophrenics experience hallucinations in the form of hearing strange voices. The disordered thought process also gives rise to a host of delusions that have devastating effect on the social lives of schizophrenics. Delusion a fixed wrong belief could be of various types. A bizarre delusion is one that is not only

very strange but its occurrence is almost impossible. For example, a Schizophrenic person may have a delusion that some parts of his/her body have been removed by strange beings or the world is coming to an end.

A non-bizarre delusion, on the other hand, could be possible but for a normal individual the belief is surely mistaken, like an unfounded belief of being under constant police surveillance. A delusion could also be a reflection of one's mood like the grim thoughts of rejection by all while being in a state of depression or having strange manic thoughts like being the Prime Minister of the country. A schizophrenic may also strongly believe that he/she has special powers or abilities and is a famous personality.

Some of the common delusions that most schizophrenics experience include the false belief that some external force or an unknown person is controlling their thoughts and feelings. Called the 'delusion of control', victims of such a delusion feel helplessly imprisoned and have absolutely no control whatsoever over their bodily movements. Such unfortunate victims are constantly troubled by the false belief that their thoughts are being heard aloud or someone is trying to insert/remove thoughts from their minds. Most schizophrenics also have a very disturbing delusion that other people can know their thoughts.

Another common delusion that schizophrenics and even most otherwise normal persons, have is the 'delusion of infidelity' that makes one strongly believe that one's spouse or lover is having an affair. On the contrary, some victims may suffer from 'erotomania' that makes them believe that another person is in love with him or her. The victims of this mental disorder also may have a 'delusion of guilt', due to which they hold themselves responsible for a crime they have never committed actually or consider themselves the cause of a natural disaster like earthquake or floods. Similarly, such persons may wrongly believe that an environmental event may have a special message for them. Other delusions that ruin the lives of schizophrenics include the belief of being cheated, harassed or

attacked by others. This delusion plunges the victim in a state of constant fear from the unknown 'other'.

Schizophrenics may also suffer from chronic depression and anxiety disorder, besides some of them being under the grip of a substance abuse. Due to their inability to take good care of themselves, many victims suffer from physical health problems and remain unemployed. A disorder in thinking invariably results in social isolation. In some cases however, victims become mute and remain motionless in bizarre postures, which is a clear-cut sign of a condition called 'catatonia'.

History

Derived from the Greek words, skhizein (to split) and phren (mind), Schizophrenia is a mental disorder that affects one's thought process. The term 'schizophrenia' was coined by Eugen Bleuler in 1908. It was first described by Benedict Morel in 1853 as a mental illness affecting teenagers and young adults. The term Dementia Praecox was used in 1891 by Arnold Pick that means 'early dementia'. Later in 1893 Emil Kraepelin also described Dementia Praecox as a disease of the brain, a form of dementia that affected young adults.

It was Kurt Schneider, a German psychiatrist who around 1950, first listed the symptoms of Schizophrenia, distinguishing them from other psychotic disorders. Called Schneider's first-rank symptoms, these include delusions and hearing hallucinatory voices. There are positive and negative symptoms. Positive symptoms are mainly delusions and auditory hallucinations, which are present in only schizophrenics. Negative symptoms are those that are not present in schizophrenic persons but are found in healthy persons, such as the inability of normal speech and expression of pleasure, lack of motivation, and having no desire to form relationships.

Diagnosing Schizophrenia

Schizophrenia affects men and women equally. It rarely occurs in children, but awareness of childhood-onset Schizophrenia is

increasing. The risk is highest for an identical twin of a person with schizophrenia. A young adult having an abnormal behaviour is confirmed to be a case of Schizophrenia based on the victim's self-reported experiences and abnormalities in behaviour reported by family members and friends. Psychiatric assessment basically includes a psychiatric history of the disorder in the family and development of typical symptoms ascertaining the possible factors that might have triggered the disease. No laboratory tests are conducted for substantiating the diagnosis as the observed behaviour itself is quite typical of this mental disorder.

The most widely used standardized criteria for diagnosing schizophrenia is based on the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, version DSM-IV-TR, and the World Health Organization's International Statistical Classification of Diseases and Related Health Problems, the ICD-10. The latter criteria are typically used in European countries, while the DSM criteria are used in the United States and the rest of the world. The three diagnostic criteria generally accepted for diagnosing schizophrenia are the following: First, the presence of at least two characteristic symptoms (delusions, hallucinations, disorganized speech, disorganized behaviour, catatonic behaviour). Second, the presence of social/occupational dysfunction that makes the victim unable to carry out normal work where interaction with family members, friends and colleagues is important. Lastly is the presence of above symptoms for at least six months.

The symptoms of Schizophrenia are quite typical, although psychotic symptoms are also present in other mental disorders, like bipolar disorder, personality disorder and drug-induced psychosis, while non-bizzare delusions are present in social anxiety disorder. Similarly, the symptoms of obsessive compulsive disorder are different from the delusions of Schizophrenia.

Analysis of brain functioning with Positron Emission Tomography (PET) a nuclear medicine imaging technique that produces a 3D image of body's functional processes has shown that a lowered frontal lobe activation of the brain during a working

memory task, poses the risk of increased activity of a neurotransmitter called 'dopamine' in the synaptic junctions where neurons meet. Besides the frontal lobes, functional differences in the brain activity of schizophrenics also occur in the hippocampus and temporal lobes. Similarly, Magnetic Resonance Imaging (MRI) and other brain imaging technologies have today revealed the clear-cut differences in the brain activity of schizophrenics.

The brains of people with Schizophrenia also look different from those of healthy people. Thanks to these imaging technologies, differences in the size and structure of certain areas of the brain in schizophrenics are clearly known today. MRI studies have shown that the volume of the whole brain and the hippocampus region are markedly reduced in schizophrenics, while the fluid-filled cavities at the center of the brain, called ventricles, are larger in schizophrenics as compared to healthy individuals.

The Cause Factors

It has been commonly observed that Schizophrenia runs in families. Besides being genetically inherited, this disorder is also found to be triggered by some traumatic experiences during early adult life. It is now also known that prenatal exposure to infections increases the risk for developing schizophrenia later in life. Besides, childhood experiences of abuse or trauma are also serious risk factors for developing Schizophrenia. Unsupportive parenting where children develop strained relationships with parents also contribute to an increased risk of this disorder. Thus, early environment plays a crucial role in the surfacing of abrupt behavioural changes in the affected persons.

Certainly, there occurs discrete biochemical changes in the brain cells/neurons of the victims that result in altered neurochemistry which is the hallmark of disintegrated thought process. The network of neurons that is spread all over the human body basically comprises billions of interconnecting neurons that pass on the neural message from one cell to the other in form of specific neurochemical signals, which are nothing but biochemical

molecules called the 'neurotransmitters'. These substances allow brain cells to communicate with each other, and are released in very precise amounts at the junctional points where the dendrites of one neuron intersect with the axon terminals of another neuron. One such neurotransmitter is called 'dopamine', which plays a crucial role in brain chemistry. It is the excessive production of dopamine that awefully disturbs the flow of information through the neural wiring, and thus plays havoc in the thought process, typical of Schizophrenia.

Many different genes seem to be involved in the abnormally raised activity of dopamine in the neurons. Certain genes linked to an increased risk of Schizophrenia have been found, which produce defective proteins that play a crucial role in altering the neural signalling. Rare deletions or duplications of tiny DNA sequences in these genes make them alter their expression, thus causing the production of a defective variant of the normal protein. It is understood today that there is an increased production of Dopamine Receptor D_2, also known as D2R, which is a protein encoded by the DRD2 gene. This is known to give rise to the positive symptoms of Schizophrenia. Therefore, most anti-psychotic drugs cause the D2 blockage or have dopamine blocking effect. However, newer anti-psychotic drugs also affect the production of another neurotransmitter called serotonin.

Indian scientists have made a mark in unravelling the genetic basis of schizophrenia, thanks to the efforts of Dr Samir K. Brahmachari, Director General CSIR and his team comprising scientists at the Institute of Genomics & Integrative Biology (IGIB), New Delhi who in 2003 identified a mutation in a gene named 'Synaptogyrin I' (SYNGR 1 gene), sitting on chromosome 22, which subtly alters the neural signaling pathway and increases individual susceptibility to schizophrenia and bipolar disorder in the Indian populations. The SYNGR1 gene has been found to be associated with presynaptic vesicles in neurons and plays a crucial role in transmitting of neural messages. Based on this novel finding, a US patent on 'Novel Primers for Screening Schizophrenia and a Method

Thereof' was granted in 2004. Similarly, another gene called 'MLC1' has also been associated with these mental disorders, which also suggests the likely involvement of a common pathway in the etiology of these disorders.

Glutamate is yet another neurotransmitter. Studies have shown that there is a reduced function of the glutamate receptor in schizophrenics. Abnormally low levels of glutamate receptors are found in postmortem brains of the victims of this disorder. Substantiating this, it has been found that glutamate blocking drugs can mimic the symptoms with Schizophrenia.

Persons at high-risk of developing this disorder include those having a family history of Schizophrenia and are undergoing some psychotic experience. Psychological treatments and medication seem to be effective in reducing the chances of such 'high-risk' people to develop full-blown Schizophrenia.

Traumatic Treatment

First introduced in the 1930s, Electro Convulsive Therapy (ECT), also called electroshock treatment has been a common psychiatric treatment in which seizures are electrically induced in anesthetized patients for therapeutic effect. This treatment is, however, rarely used as a first-line treatment for Schizophrenia and is only considered after long, unsuccessful treatment with anti-psychotic drugs.

Another shock therapy commonly used in the hospitals during the 1940s and 1950s was 'insulin coma therapy'. This psychiatric treatment involved the injection of large doses of insulin that induced symptoms of reduced blood sugar (pallor, perspiration, salivation, restlessness) and resulted in coma if the dose of insulin was high. Horrifyingly, patients were subjected to several comas with reducing dose of insulin, before the treatment was stopped. It is no longer practiced now.

Psychosurgery or neurosurgery for mental disorders was first introduced in 1930s. It basically involved the operation, under

general anaesthesia where a small piece of brain tissue was destroyed or removed by thermo-coagulation, freezing, cutting or using radiation. Another neurosurgical method to treat schizophrenia has been 'deep brain stimulation', where specific areas of the brain are stimulated with implanted electrodes. Although patients do show improvement in their symptoms after neurosurgical treatments, these methods are not a recommended treatment.

Special class of drugs called as anti-psychotic drugs help in the treatment of Schizophrenia, as they work by suppressing dopamine activity inside the neurons. It was in 1950 that the drug chlorpromazine – the first drug developed with anti-psychotic action – was synthesized. This drug indeed brought a revolutionary advance in the treatment of Schizophrenia, as hospitalization could be avoided and social rehabilitation of such persons could be done to a great extent. Chlorpromazine – a 'benchmark' drug in the treatment of Schizophrenia – works on several receptors on neurons, blocking the activity of neurotransmitters that act by binding to those receptors. The side effects of this drug include sedation, constipation, hypotension and restlessless. Long term or high dose use of the drug can cause involuntary, repetitive body movements or tremors called 'tardive dyskinesia', a condition that is reversible. Similarly another drug group, which blocks dopamine function is called 'phenothiazines', which can reduce psychotic symptoms.

Today, however, there are more effective anti-psychotic drugs available. Clozapine is the first of a typical anti-psychotic drug used in the treatment of schizophrenia that was first introduced in Europe in 1971. Although a highly effective drug to treat Schizophrenia, it unfortunately causes a drastic reduction in the number of white blood cells, a condition called agranulocytosis, which can prove fatal. In 1989, the US FDA approved the use of clozapine for only treatment-resistant Schizophrenia, or patients not responding to other anti-psychotic treatments. However, periodic blood testing for patients taking clozapine was made essential to monitor the adverse effects of this drug on the patient.

Risperidone, first released in 1994, is also a common atypical anti-psychotic drug used to treat Schizophrenia. However it induces weight gain and sexual dysfunction besides having the other side effects common to most anti-psychotic drugs. Similarly, another atypical anti-psychotic drug, olanzapine is also associated with considerable weight gain and risk of metabolic syndrome.

Studies have shown that a vast majority of schizophrenics use drugs, alcohol or tobacco, which is suggestive of the victim trying to cope with unpleasant states like depression, anxiety, boredom and loneliness. Substance abuse can make treatment for schizophrenia less effective. In fact, research has found increasing evidence of a link between marijuana and Schizophrenia symptoms. Similarly, smoking tends to make anti-psychotic drugs less effective.

Above all, vocational and social rehabilitation are very important for making schizophrenics lead a less traumatic life. Public education campaigns also assume great importance for reducing the burden of this disorder on human populations, as information about risk factors and early symptoms of this mental disorder can help in timely treatment and social rehabilitation of the affected persons.

Psychotherapy is personal counselling of the patient, aimed at increasing the sense of their own well being. This involves several relationship-building techniques like friendly communication and dialogue for bringing about a behavioural change in the victims. Techniques like cognitive behavioural therapy and cognitive remediation help to treat psychotic symptoms, and improve social rehabilitation of schizophrenics.

Positive Approach

The World Health Organization (WHO) coordinated the International Study of Schizophrenia (ISoS) – a long-term follow-up study of 1633 individuals diagnosed with schizophrenia around the world – and published the findings in 2001. The results shook the prevalent belief that schizophrenia is a chronic mental illness.

Of the 75 per cent who were available for follow-up, half had a favourable outcome, and 16 per cent had a delayed recovery. It clearly came out that early social intervention was essential for improving patient condition. WHO studies have also shown that individuals diagnosed with schizophrenia have much better long-term treatment outcome in developing countries including (India, Colombia and Nigeria) than in developed countries that include USA, UK, Japan, and Russia. Scientists have learnt a lot about schizophrenia, but more research is needed to provide answers to many still unexplained facts. For this, more funding is needed to promote mental health research.

A Rare Accomplishment

It is quite astonishing that a person diagnosed as schizophrenic during college years has the interest to continue his studies, so much so that in later life he is admired for his rare talents in the field of mathematics and is awarded the Nobel Prize for his unique contributions to the field. This man was none other than John Nash, a well acclaimed US mathematician, a victim of schizophrenia, who won the 1994 Nobel Prize in Economics. His life has even been depicted in a film, A Beautiful Mind.

World Mental Health Day

On October 10 every year, World Mental Health Day is observed in more than 100 countries. Celebrated since 1992, this event is an initiative of the World Federation for Mental Health (WFMH) and is supported by the World Health Organization (WHO). Several activities organized at both regional and National level include educational lectures and various advocacy programmes to raise public awareness on mental health issues, besides investing in prevention and treatment services.

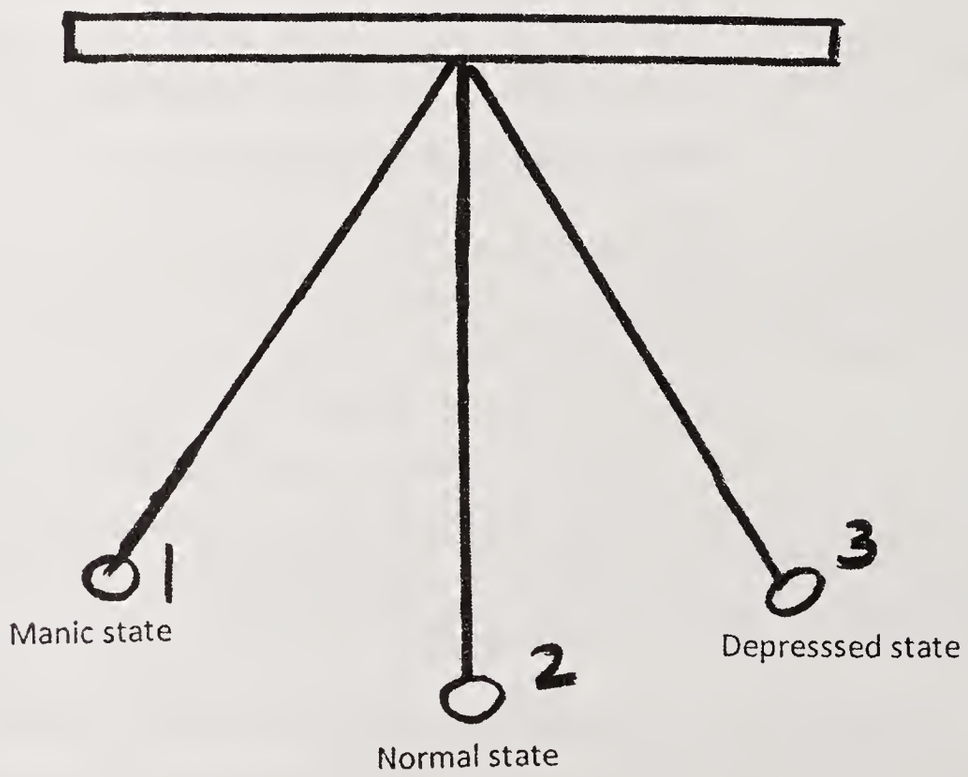
Today, most psychiatrists agree that about one-third of schizophrenia cases are curable. A positive approach for integrating schizophrenics back into the web of society is the 'family therapy' where all the family members of an individual diagnosed with

schizophrenia are appropriately informed about this mental illness and how a congenial family atmosphere can contribute towards better improvement in patient's condition. Such advocacy efforts for educating families to improve patient care at home, through compassionate understanding of this mental disorder, can avoid unnecessary hospital visits and even reduce the drug dose of such patients.

It ultimately rests with the 'sane' individuals of the family and society as a whole to remove the stigma associated with schizophrenia and accept their less fortunate brothers and sisters suffering from this disorder as an integral part of family/society, and provide them a supportive and tolerant environment that naturally draws such people back into the social network.

Bipolar Disorder

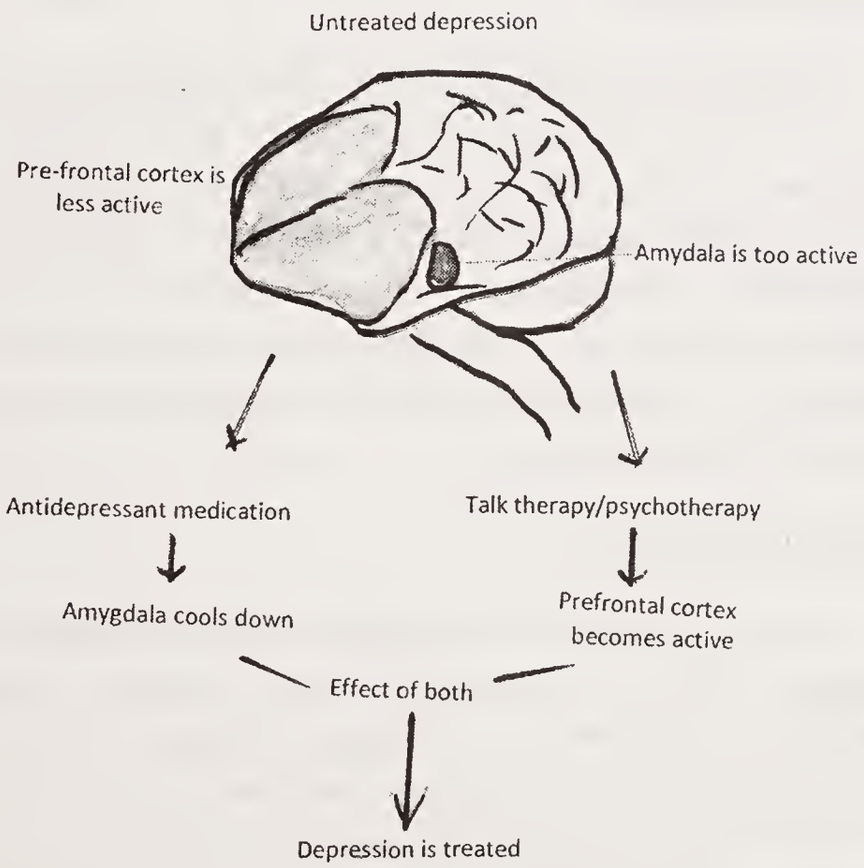
The sufferers of this mental disorder constantly swing through periods of manic and depressive states that ruin their social and family life. Also called manic-depression, the manic episodes are



Abnormal chemical signalling between neurons is the cause of all psychosomatic disorders like mood swings between manic and depressed states.

characterized by elevated or irritable mood, increased energy, decreased need for sleep, poor temper control and irresponsible behavior while the depressive episode is marked by loss of energy, feelings of sadness, guilt, low self-esteem, and thoughts of death and suicide. Having such mood swings is the hallmark of this disorder, where going back and forth between mania and depression can be very quick or may last from days to months.

Family members and caregivers are very important in the treatment of bipolar disorder. In addition, a healthy diet and proper sleep can remarkably help the victims. Drugs used to treat bipolar disorder include mood stabilizers, anti-seizure drugs, anti-psychotic drugs, anti-anxiety drugs and anti-depressants. However, Electro Convulsive Therapy (ECT) may be used to treat the manic or depressive phase of bipolar disorder if it does not respond to medication. Transcranial Magnetic Stimulation (TMS) uses high-frequency magnetic pulses to target affected areas of the brain.



In acute depression, amygdala is hyperactivated and brain's prefrontal cortex is not active enough

Bipolar disorder is believed to have a genetic link as it tends to run in families. However, environment plays a significant role on the onset of this mental sickness as it takes root in the early years of childhood. Brain imaging studies have also shown abnormal patterns of brain development in children with bipolar disorder.

Obsessive Compulsive Disorder

Obsessive Compulsive Disorder (OCD) is basically an anxiety disorder where the victims are troubled by unwanted and repeated thoughts and actions called 'obsessions' which they seemingly cannot get rid of due to lack of self control. This disorder usually develops in young adulthood. Some of the probable causes of OCD are believed to be head injury and infections. The distressing obsessions or compulsions typical of OCD that interfere with daily life include checking and rechecking actions like turning out the lights and locking the door, repeated hand washing due to obsessive fear of germs, etc.

Treatment normally includes anti-depressants, anti-psychotics and benzodiazepines among other medications. Cognitive Behavioral Therapy (CBT) has been shown to be the most effective type of psychotherapy for OCD. Through this therapy, the patient is exposed to situations that trigger the obsessive thoughts, in order to develop tolerance to anxiety and resistance to the obsessive compulsion. Medication and CBT together give better results in treating OCD patients.

Drug Addiction

Compulsive use of a drug like cocaine, despite its negative or dangerous effects, is called addiction. However, a person may be physically dependent on a substance without having an addiction. Like medicines to control blood pressure are not addictive but they do cause physical dependence. Drug abuse can lead to drug dependence or addiction. Tolerance to a drug is usually a part of addiction. Drug abuse may be a result of peer pressure, stress, anxiety, depression and emotional weakness. Addictive drugs

include opiates and narcotics that are powerful painkillers like heroin, opium, codeine etc; Central Nervous System (CNS) stimulants like cocaine, amphetamines etc; CNS depressants like alcohol, barbiturates, benzodiazepines etc; Hallucinogens like LSD, mescaline etc; Tetrahydrocannabinol (THC) present in marijuana (cannabis) and hashish. Drug use normally starts as experimental use of a drug that takes the form of regular use, turning into a habit of daily consumption and slowly the stage of dependence is reached.

The typical behavioural symptoms of drug dependence include confusion, inability to stop drug intake, missing work that reduces performance, secretive behaviour and reduced diet. Some serious complications of addiction may be drug overdose, depression, occurrence of cancer, HIV infection, problems with memory/ concentration and unsafe sexual practices. Stopping drug use and staying drug free consciously is the best treatment to get rid off the menace of addiction. Counselling, psychological intervention and medication are all important components of treatment that restore normalcy in the lives of persons once misled by circumstances.

All psychiatric and psychosomatic disorders ranging from Schizophrenia, Bipolar Affective Disorder and Manic Depression to Obsessive Compulsive Disorder and even drug addiction occur due to a breakdown of the neuronal machinery. The hallmark of these pathetic illnesses that render their victims a prey of odd/ disturbed thought processes is the interplay of several chemical signals, in the form of neurotransmitters, as they are produced in abnormally high or low levels which resultantly, transmits wrong messages to and fro in the neural networks.

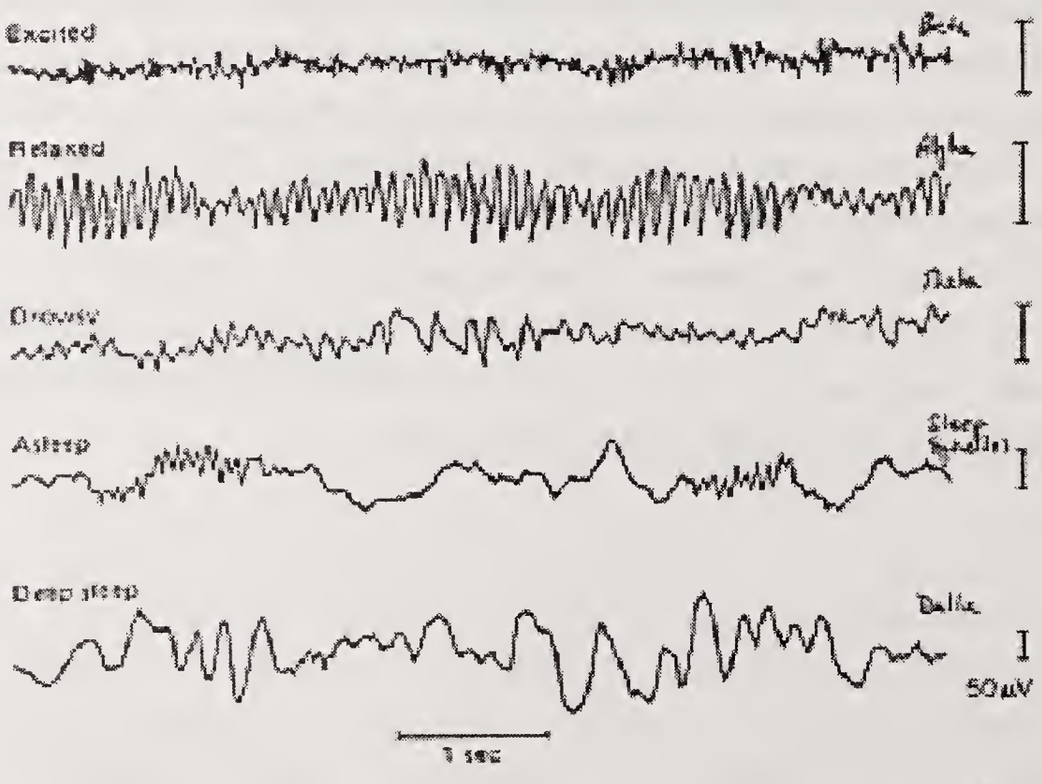
6

Peering into the Brain

A peep inside the human brain can reveal amazing facts about Iits electrical activity and blood flow through its various parts, as this marvellous organ of intellect responds to stimuli. Any changes in its proper functioning thus come to light that may be responsible for a mental sickness. Thanks to modern medical technologies, it is possible to map and monitor the brain's activities to ascertain the cause of altered brain functions.

Electroencephalogram (EEG)

One of the best known methods to record the electrical activity of human brain is the Electro Encephalogram (EEG). This method



The electric activity of brain is recorded as wavy lines on EEG. The picture shows different types of brain waves

employs special sensors called electrodes which are attached to the head and hooked by wires to a computer. The latter records the brain's electrical activity on the screen or on paper as 'wavy' lines, which show changes in their normal pattern in persons having an anomaly in brain functioning.

The neural activity produces tiny electrical signals called impulses. This electrical activity of the brain is seen as different types of waves: Beta waves have a frequency of 13 to 30 cycles per second, which normally occur in wakeful state. Alpha waves having a frequency of 8 to 12 cycles per second occur when the body is more relaxed, with eyes closed, but one is mentally alert. Theta waves have a frequency of 4 to 7 cycles per second, which are normally found when one is asleep. Similarly, Delta waves that have a frequency of less than 3 cycles per second are found when one is in deep sleep.

EEG is usually done to diagnose epilepsy and the type of seizures that occur in a patient. It is also used to find the underlying cause for the loss of consciousness and studying the abnormal brain activity in sleep disorders, diseases like Alzheimer's and head injuries, while monitoring the brain activity during brain surgery. EEG would reveal no brain activity when the brain function stops, as in coma, due to lack of oxygen or blood flow inside the brain.

Computerized Axial Tomography (CT Scan)

Computed Tomography makes pictures by sending many X-rays through the body and taking views from many different angles. Thus cross-sectional images of the bones and soft tissues of the body can be generated, which help in viewing all parts of the body from different angles. This technique is commonly used to examine patients who have had internal injuries like victims of car accidents etc. This non-invasive technique helps to diagnose several medical conditions like bleeding in the brain or haemorrhage, brain tumour, sinusitis, stroke etc.

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging uses powerful magnets and pulses of radio wave energy to take pictures of the body. It can reveal tissue damage or disease, such as infection, inflammation or a tumor in the body. MRI of the head is done, in many cases, to look for the cause of headaches. It can help to diagnose brain stroke and other conditions related to improper blood flow in the brain.

MRI is also done to ascertain changes in the brain in diseases like Huntington's disease, Multiple Sclerosis (MS), Parkinson's disease and Alzheimer's disease. Besides, this technique is highly useful in diagnosing birth defects of the brain, infection and tumours, in addition to understanding the cause of muscle weakness or numbness/tingling vision, speaking and hearing difficulties. As MRI does not use any radiation, it does not pose any risk as there are no side effects from magnetic fields and radio waves. However, strong magnetic fields can affect the working of heart pacemakers and other implants.

Positron Emission Tomography (PET)

It is a powerful imaging technique used in the diagnosis of many diseases, particularly cancer. This non-invasive test, popularly called 'PET scan' accurately images the body's physiological/functional changes, while a Computed Tomography or 'CT scan' shows the structure of the anatomy where the changes are taking place. A highly sophisticated PET/CT imaging technique combines these two tests and thus provides detailed information about the presence or spread of disease and also identifies its precise location in the body. For patients undergoing treatment, a PET/CT scan can provide information on the extent of the progress made.

Basically, for PET scan a radiotracer molecule is first inserted into the human body, which comprises a radioactive medicine tagged to a natural chemical like glucose. This radiotracer finds its way into tissues that use the natural chemical. As the radiotracer breaks down inside the patient's body, sub-atomic particles called

'positrons' are made that are detected in PET scan in the form of three-dimensional pictures. This imaging technique is helpful in diagnosing diseases like epilepsy, Alzheimer's disease, cancers and heart ailments. Pregnant and lactating women should not have a PET scan as it could be harmful for the baby. The body's vital functional aspects like blood flow, oxygen use, glucose metabolism etc., can be measured in PET scan that reveals metabolic changes occurring in tissues and organs.

Notwithstanding the tremendous advances in imaging of the human brain, the mysteries about its functioning and cellular alterations in disease and injury abound. There is a vast arena of ambiguity that surrounds the understanding of the human brain. Therefore, the search for devising newer and better technologies for seeing the inner confines of the human brain is on.

7

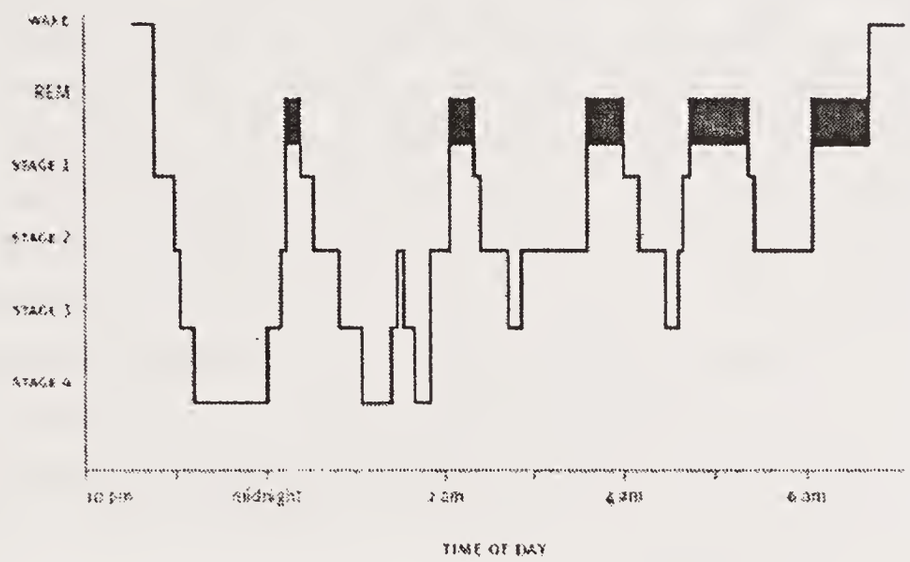
Brain Rejuvenator
A Good Night Sleep

A long day of hard work and mental stress may diminish one's vitality which can be only restored by a good night sleep. Having rested undisturbed, the body normally comes back to its normal state of energy, just as the dawn of a new day brings in fresh life and hope for all. However, everyone is not so lucky to have a peaceful, uninterrupted sleep night after night as many people suffer from sleep disorders and have a disturbed sleep pattern. Insomnia or lack of sleep also drains away the body's energy and disrupts the sleep and wake time, thus making one feel quite sick.

As we trace the patterns of sleep, it is indeed astonishing that while we sleep, our brain buzzes with activity. This brain activity can be recorded as Electro Encephalograms (EEGs) which reveals the dynamic behaviour of sleep manifested as characteristic electrical patterns in a sleeping person's brain as well as the presence or absence of eye movements. Based on this, the two main types of sleep are Rapid-Eye-Movement (REM) sleep and Non-Rapid-Eye-movement (NREM) sleep. On an EEG, REM sleep is called the active sleep that is characterized by low-amplitude high-frequency waves having 'alpha' rhythm. The eye movements of REM sleep are believed to be related to dreams, as people who are awakened from REM sleep normally report their dreams in a vivid manner.

On the other hand, in NREM sleep, there are three distinct stages: N1, N2, and N3. During the progression from stage N1 to N3, brain waves become slower and more synchronized. Therefore,

in stage N3, EEG reveals high-amplitude, low-frequency waves (delta waves) that is characteristic of deep sleep. Normally, in a healthy adult, sleep begins with NREM sleep where the transition from wakefulness to N1 occurs within seconds after the slow eye movements appear in a person who is feeling very sleepy. The second stage, or N2, comes next that lasts for 10 to 25 minutes, which then progresses to N3 stage. The latter is deep sleep that lasts for 20 to 40 minutes.



The pattern of sleep

As NREM sleep progresses, the brain becomes less responsive to external stimuli, and it is difficult to awaken an individual from sleep. The REM sleep follows this, which comprises about 20 to 25 per cent of total sleep in a typical healthy adult. NREM sleep and REM sleep continue to alternate through the night in a cyclical fashion. Interestingly, most NREM sleep occurs in the first part of the night. Although the first episode of REM sleep may last only about five minutes, it generally becomes longer through the night. The normal cycles of NREM and REM sleep are believed to restore both physical and mental states of the body on waking up. Normally, younger people have more concentrated periods of deep sleep and older people have more periods of REM sleep. Sleep patterns can be affected by many factors like age, stress, alcohol, drugs,

environmental conditions such as temperature and light, and time of the day or night relative to an individual's internal/biological clock. Normally, the intake of coffee, tea, chocolate or cola drinks at bedtime interferes with sleep. Whereas, herbal oils such as juniper, lavender, geranium, sandalwood, neroli and ylang ylang help to induce sleep.

Dreams are believed to be the expressions of deep-seated emotions that to some extent are precognition about the future. According to Sigmund Freud's theory of dreams, dreams are a representation of unconscious desires, thoughts and motivations. The activation-synthesis model of dreaming, proposed by J. Allan Hobson and Robert McClarley in 1977, emphasizes that certain neural circuits in the brain become activated during REM sleep, which in turn, activates specific areas of the limbic system involved in emotions, sensations and memories, including the amygdala and hippocampus. The brain's interpretation of this neural activity during sleep is manifested as dreams. However, there are several other theories that provide suggestive explanations to the occurrence and meaning of dreams.

Sleep disorders are changes in sleeping patterns, which may range from excessive daytime sleepiness and increased movement during sleep to difficulty in sleeping and abnormal sleep behaviours. Insomnia is the most common type of sleep disorder where a person is unable to get proper amount of sleep one needs to wake up refreshed. It, however, is often a symptom of another problem like stress, anxiety, depression, jet lag and intake of some drugs among other factors. In addition to insomnia, the most common sleep disorders are sleep apnea, Restless Legs Syndrome (RLS), and narcolepsy.

Respiration and sleep are strongly coupled. Changes in the neurological control of breathing are known to affect sleep patterns and this may result in periodic breathing, upper airway obstruction besides sleep apnea periods. Sleep apnea is a breathing disorder characterized by brief interruptions, for over 10 seconds, of breathing during sleep that can occur up to hundreds of times a

Medical science has made great advances in understanding the working of the cellular machinery of different organs of the human body. But the present knowledge of functional intricacies of the human brain is still inadequate. No wonder, the root cause of many afflictions of the brain and mind remains an enigma and their cure a far cry.

Written in an easy-to-understand style, this book provides answers to many mind-boggling questions - How the primordial brain cells in a foetes grow and develop? In what way the genetic material one is born with and the adaptations and learning from the environment contribute to brain development? It also explains common brain afflictions, while highlighting the role of good night sleep, positive thinking and mind relaxation techniques.

Dr. P. Cheena Chawla, a Doctorate in Biotechnology worked with Council of Scientific and Industrial Research (CSIR) for more than 22 years and was associated with National Institute of Science Communication & Information Resources (NISCAIR). She has written a number of books on popular science and more than 500 popular articles on biotechnology. Dr. Chawla's work in the field of science popularization has been recognised nationally through a number of awards conferred on her.

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